

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

EDITED BY
SIR WILLIAM HALE-WHITE, K.B.E., M.D.
AND
T. WATTS EDEN, M.D.
UNDER THE DIRECTION OF
THE EDITORIAL COMMITTEE

VOLUME THE NINETEENTH
SESSION 1925-26

PARTS I & II
GENERAL REPORTS JOINT DISCUSSIONS

SECTIONS:—

ANÆSTHETICS	BALNEOLOGY AND CLIMATOLOGY
CLINICAL	COMPARATIVE MEDICINE
STUDY OF DISEASE IN CHILDREN	DERMATOLOGY
ELECTRO-THERAPEUTICS	EPIDEMIOLOGY AND STATE MEDICINE
	HISTORY



LONDON
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DEATH OF SIR JOHN MACALISTER.

It is with the deepest regret that we have to announce the death of our late Secretary and Editor, and Honorary Fellow, Sir John Mac Alister, F.S.A., who passed away peacefully at his residence, 33, Finchley Road, N.W. 8, on Tuesday evening, December 1, after long illness.

We can do no better than quote the resolution passed at the Meeting of the Council held on Tuesday, December 15 :—

That the President and Council of the Royal Society of Medicine wish to record their deep gratitude for the selfless devotion of Sir John Mac Alister to the Society during the thirty-eight years in which he held office as Secretary, their sense of the great loss which the Society has sustained in the death of their esteemed and loved Secretary and Honorary Fellow, and to express to his family the Council's sympathy with them in their bereavement.

This resolution was moved by the President from the Chair, and passed while all those present stood in respect of the memory of one who had done so much for the Royal Society of Medicine.

A Memorial Service was held at St. Peter's, Vere Street, W., on Saturday, December 5, at which there was a large attendance of Fellows and Members of the Society.

EXTRACT FROM THE PRESIDENT'S SPEECH at the ANNUAL DINNER of the SOCIETY held on November 19, 1925.

"The last session has been an eventful one in the history of this Society—the most eventful perhaps since, in 1907, it attained its full stature by the amalgamation of the eighteen different medical societies then existing in London. The man who achieved that had been our Secretary since 1887—thirty-eight loyal years. During these he wrought for us three great and successful achievements. The first was the removal of the old Medico-Chirurgical Society from two or three stuffy rooms which lodged it in Berners Street to a building in Hanover Square. The second was the federation of these eighteen societies into this, our Royal Society of Medicine, the largest of its kind in the Kingdom and with the most complete medical library in the Empire.

The third great feat of our devoted Secretary was the erection of the Society's handsome house in Wimpole Street. When our friend first joined our service we had 745 Fellows ; we now have 4,000. Our annual income was £1,676 ; it is now £19,000. Our *Proceedings* were printed in two handy volumes and cost £406. To-day, they run to 1,232 pages and cost £4,000 a year.

Last Session the Society and its Sections held 171 Meetings and Discussions, attended by 6,800 Members ; the Library was visited by 20,718 readers, 13,734 books were taken out, and 3,054 parcels of books were sent, carriage free, to our Fellows in the provinces and abroad.

These thirty-eight years of Sir John Mac Alister's active, ungrudging and loyal service came to an end last Christmas. Ill-health compelled a long leave of absence and during this he felt obliged to send in his resignation which took effect at the end of June.

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The Royal Society of Medicine.

President—Sir STCLAIR THOMSON, M.D., F.R.C.S.

DISCUSSION ON FOCAL SEPSIS AS A FACTOR IN DISEASE.

Professor GEORGE R. MURRAY, M.D.

DURING recent years much attention has been drawn to the subject selected for discussion to-day, and we have learned how important a part focal sepsis may play in the causation of disease and in the progress of a malady already present. In order that we may as far as possible have a definite idea of what we are discussing, I propose to outline the various modes by which focal sepsis may become a factor in disease. These will be illustrated by a few brief clinical sketches of personal experiences, in most of which, owing to the circumstances under which they occurred, no bacteriological examination was made.

A malady may be initiated or its course affected by a local infection in several different ways. First, the bacteria causing the focal infection may be discharged and conveyed by mechanical means so as to cause extension of the disease by re-inoculation. Second, the bacteria present in the original focus may overcome the local resistance and be conveyed to distant parts of the body by way of the lymphatics and the blood. Once the bacteria leave the original focus, either singly or in clumps, they may be arrested by the nearest lymphatic gland and set up a lymphadenitis which may develop into an abscess. If the infection passes this barrier three things may happen: (a) If the organisms are virulent they may multiply in the blood and set up either an acute or chronic septicæmia; (b) if the bacteria do not multiply in the blood they may be conveyed alive to a suitable nidus where they multiply and infect the surrounding tissues; (c) the bacteria conveyed by the blood are unable to gain a real footing anywhere; they may, by the process named subinfection by J. G. Adami [1], produce a slow but progressive atrophy with replacement fibrosis in various organs of the body. Thirdly, the micro-organisms may remain enclosed at the seat of focal infection from which their toxins are slowly and continuously absorbed so as to cause either temporary alteration in the structure and function of the blood and other tissues, or possibly permanent structural changes in important organs.

A few practical illustrations of the influence of focal sepsis will be given under the headings just mentioned. The results of the mechanical conveyance of infection are seen in a simple form in a case of furunculosis, in which the staphylococci are conveyed by the fingers or by the clothing from the primary boil to other parts of the skin where re-infection takes place. In open oral sepsis, due either to the decomposition of food particles or tartar deposited in the gingival trough, or to pyorrhœa resulting from chronic periodontitis, bacteria are constantly brought into contact with the tongue and pharynx, and may set up superficial glossitis or pharyngitis. Infection is occasionally conveyed up Stenson's duct to the parotid gland. Thus, I have seen a man who was laid up with a unilateral parotitis which persisted until it was realized that it was due to an ascending infection from a septic molar

tooth situated near the opening of Stenson's duct. As soon as the tooth was removed the parotid gland recovered.

In both oral and naso-pharyngeal sepsis many bacteria are swallowed. In a normal stomach they are usually destroyed by the gastric juice. In a small proportion of cases the resistance of the stomach is impaired and a chronic gastritis or gastric ulcer develops.

A man aged 58 gradually lost his appetite, the weight decreased by 3 st., and there was vomiting. When I saw him he was lying in bed weak and emaciated, and the skin of the face and neck was pigmented, so that the symptoms were suggestive of malignant disease of the stomach. Physical examination yielded no sign of abdominal or thoracic disease, but revealed marked oral sepsis. A diagnosis of septic gastritis was made and proved to be correct, as treatment by the immediate use of an antiseptic mouthwash, removal of the teeth, and the internal administration of manganese dioxide was followed by complete recovery in the course of a few months.

The infection arising from oral sepsis may pass through the stomach and cause infection of either small or large intestine.

A boy, who was seen some years ago, was in poor general health owing to severe oral sepsis. The relations were advised to have the teeth removed at once and were warned of the danger of delay. Unfortunately, extraction of the teeth was refused, and a few months later the boy developed severe ulcerative colitis and died.

A septic gall-bladder, by discharging bacteria along the common bile-duct, may infect the bowel lower down. In the case of infection of the gall-bladder by the typhoid bacillus the host becomes either a temporary or chronic "carrier," and so a source of infection which may set up typhoid fever in others. The long duration of this focal infection in some cases is illustrated by the records of "carriers" mentioned by Professor Topley [2] who have continued to infect the healthy for as long as twenty-five years. An infected but still patent appendix may cause ill-health by continually discharging its contents into the cæcum. Sir Rickman Godlee [3], in one of the earliest papers dealing with this subject, recorded such a case in which the chief symptoms were pallor, loss of appetite, loss of weight, slight fever, and the passage of offensive motions. Complete recovery followed the removal of the diseased appendix. Infection from the mouth may pass directly, not only to the alimentary canal but to the respiratory organs.

A woman, on account of dental sepsis, had several teeth extracted while under general anaesthesia. During, or just after, the operation she unfortunately inhaled either some inspissated pus, or possibly a small fragment of an infected tooth, into a bronchus. This set up an acute local infection of the lung which, by the time I saw her, had become gangrenous and shortly afterwards proved fatal.

When bacteria which at first have been confined to a local area find their way into the blood a general septicæmia may result. This sequence of events has occurred only too frequently in those tragic cases in which a surgeon during an operation, or a pathologist while making an autopsy, has received a slight wound which has become infected, and the infection spreading later to the blood has caused a fatal septicæmia. Micro-organisms which gain access to the blood may be unable to multiply until they reach some tissue for which they have a selective affinity, and in which they can multiply sufficiently to set up a definite lesion.

A healthy young farmer, in the course of a quarrel, received a wound in the forehead from a tumbler which was thrown at him. The wound was dressed at once by a surgeon. He returned to his work on the farm, but took no further care of the wound. This became infected, probably by his hands while at work, cellulitis of the neck followed, and finally acute malignant endocarditis ended a promising career.

In closed oral sepsis, such as occurs when an abscess forms at the root of a

tooth, streptococci may be forced into the general circulation by the intermittent pressure exerted on the tooth during mastication. Under these circumstances the streptococci are liable to be lodged in the joints or periarticular structures. When we are confronted by an arthritis, or some other malady, which may be caused by secondary infection from some occult focus of sepsis, and in which the mouth looks harmless, let us not "forget the poisonous dregs that lurk beneath," but insist on an X-ray examination of the gums.

A middle-aged man, who for some time had resided in another country, consulted me on account of an early arthritis which had already involved several joints. He assured me that his teeth had been well looked after and were in good condition. On inspection the gums looked healthy, but many of the teeth were crowned with gold. An X-ray examination revealed the presence of abscesses at the roots of several teeth. Removal of the affected teeth was at once followed by rapid improvement in the arthritis.

Sir William Willcox [4] has shown the frequent relationship between oral sepsis and arthritis, and agrees with Dr. A. P. Beddard that 90 per cent. of cases of rheumatoid arthritis in man are due to this cause. Rosenow [5] has shown that muscular fibrositis may be caused by the lodgment of streptococci of low virulence in the capillaries which are near the tendinous insertions of the affected muscles. This is apt to occur when the original focal sepsis is due to the *Streptococcus viridans* and other non-hæmolytic strains, the actual lesion in the muscle being due to subinfection. The relationship between oral sepsis and severe secondary and pernicious anæmias has been shown by Dr. William Hunter [6] to be of frequent occurrence. Focal sepsis is not, however, the only cause of these conditions, as pernicious anæmia develops in persons who have been toothless for years and in whom no septic focus can be found. In connexion with the affinity of streptococci for the joints and periarticular structures, the work of Rosenow may again be quoted. He showed that streptococci cultivated from a septic focus in man had an elective affinity for the same tissue in a healthy animal as that from which they had been taken. Thus, streptococci taken from a cholecystitis were, on inoculation, much more likely to reproduce the same condition than any other lesion. He also found some evidence in favour of the view that the toxins produced by the streptococci may exercise a similar selective action on the tissues.

Rosenow suggests that this selective action may depend on the amount of oxygen and food supply available in different parts of the body, as each strain of streptococci has its own special requirements. This peculiarity may be one of the factors which fortunately enable many persons to resist secondary infections and the ill-effects of toxæmia altogether, or at any rate for long periods.

This resistance, in the case of oral sepsis for example, may partly be due to a tolerance acquired by the long-continued presence of large numbers of streptococci in the mouth and in the bowel of normal individuals. Sir Frederick W. Andrewes [7] has drawn attention to Dr. Gordon's examination of the buccal secretions which in healthy human beings were found to contain from ten to one hundred million streptococci to the cubic centimetre. In the bowel, where the *Bacillus coli* group and streptococci predominate, Houston has found that the latter may exceed the former, and be present to the number of one thousand million per grm. of the fæces. When we recollect that one quarter of the fæces consists of bacteria, a large proportion of which are dead by the time they are voided, we can realize how great is the natural resistance to such inhabitants as long as they are outside the tissues. When ill-effects occur they are due to the virulence and numbers of bacteria which cause the development of focal sepsis, or to a lowering of the resistance of the host, or to a combination of both factors.

The joints are not the only structures liable to suffer from metastatic infection from the gum or the tonsil. During an epidemic of streptococcal tonsillitis in a

Lancashire town I saw a young man suffering from acute nephritis which had followed an attack of tonsillitis. Streptococci were present in the urine, so that the nephritis was evidently secondary to the focal sepsis in the tonsil. This epidemic affected a considerable number of people, but, as far as I could ascertain, nephritis was quite an exceptional complication. Not only may metastatic infection originate from a septic focus, but it may continue to be active as long as the primary focus is allowed to remain. In these cases it seems probable that the secondary infections are being continually reinforced or renewed from the primary focus.

A striking example of this persistent effect of focal sepsis in a case of rheumatism has been communicated to me by Dr. C. P. Lapage, who will publish full details. A boy, aged 10, continued to suffer from recurrent attacks of rheumatism with sore throat, fever, severe mitral endocarditis and unusually large subcutaneous nodules. Treatment by rest, salicylates and change of climate failed and so, finally, the tonsils were removed. After this there was no recurrence of sore throat, the nodules disappeared and cardiac compensation developed so well that he was able to go to school five years after the first illness. It is important to remember that if the focal sepsis remains undetected and unrelieved it may continue to exert its evil influence on health over long periods.

Godlee described a case in which several sequestra, which were ultimately discovered in the femur, had caused recurrent abscesses at intervals for forty years.

So far, the relationship between focal sepsis and the disease attributed to it is fairly clear. This relationship is more difficult to prove when there is no actual metastatic infection, but the morbid process is due to the action either of exotoxins formed locally and conveyed to other parts of the body, or of endotoxins liberated in cases of subinfection during the dissolution of the bacteria lodged in the tissues. In many cases it is not possible to distinguish between these two processes. One form of disease—amyloidosis—affords an example of definite tissue changes resulting from the continued absorption of toxins from a septic focus.

A boy, whom I saw with a country practitioner long since deceased, suffered from an empyema unrecognized until it began to leak through a small orifice just below the left nipple. The only treatment which had been attempted was the insertion into the sinus of a piece of the fine rubber tubing commonly used in association with Southey's tubes, which only allowed the pus to escape in drops. The liver and spleen were greatly enlarged owing to amyloid infiltration. Efficient drainage of the empyema was followed by recovery, and though I did not see the boy again I was informed that ultimately the enlargement of both liver and spleen disappeared. Godlee recorded a similar case in which a small but imperfectly drained empyema caused lardaceous disease of the liver and kidneys with marked clubbing of the fingers. Free drainage led to the closure of the empyema and this was followed by disappearance of the clubbing of the fingers and of the lardaceous disease, except for an occasional albuminuria. In another of his cases a patient with long standing empyema had refused operation, and pulmonary osteo-arthritis developed. This condition disappeared after the empyema had ruptured and discharged through a bronchus.

Chronic ill health or severe and acute illness may be due to the absorption of toxins from an unsuspected source, and Godlee showed the importance of hidden drops of pus, the unseen pus that "walketh in darkness and wasteth at noonday." It is remarkable that even a large septic focus may be the unsuspected source of an illness.

This was well illustrated by the case of a man who was acutely ill with a high and irregular temperature and other indications of a severe toxæmia for which no cause had been found. He had a cystic goitre which had been present for a long time, but had caused no special inconvenience. On examining the patient I found that the goitre yielded a resonant note on percussion and suggested that this curious sign was due to infection of the cyst by the *Bacillus coli*, which is a gas-forming organism, and that this local infection was the cause of the toxæmia. I know it may be objected that there is as yet no definite proof that the *Bacillus coli* produces exotoxins. It should, however, be remembered that the existence

of streptococcal exotoxins has only been recently proved. When the cyst was opened it was found to contain gas and pus which gave the characteristic smell that indicates the presence of the colon bacillus. No bacteriological examination was made, so that there may have been a mixed infection, but the rapid recovery which followed drainage of the cyst clearly indicated the relationship of the infected cyst to the illness.

In cases of oral sepsis the disappearance of anæmia, lassitude, and other signs of toxæmia on the removal of septic teeth, before the insertion of artificial dentures, is regarded as sufficient evidence that the ill health was due to sepsis and not to dental deficiency. While mentioning the beneficial results which usually follow the removal of a septic focus, it may be pointed out that there may be more than one focus, and also that focal sepsis may not be the only cause of the symptoms in any particular case, so that other foci and conditions must be looked for if the expected improvement does not follow the removal of a septic focus. The treatment of a septic focus is not altogether free from danger. An acute temporary exacerbation of the symptoms frequently follows the removal of septic teeth owing to the absorption of an extra dose of bacteria and their toxins during the operation. Occasionally this has been followed by hæmic infection and fatal septicæmia. Godlee mentions cases where the opening of an abscess, which up to the time of the operation had caused no serious disturbance of health, was followed by a fatal result.

We know very little of the effect of focal sepsis on the pregnant woman and the unborn child. The results of dental sepsis in the nursing mother have been described by H. Waller [8]. He shows that the secretion of milk may be diminished to one-half, so that the child's weight remains stationary or increases very slowly. In addition, the child shows dislike of the milk and is sick. After removal of the teeth, lactation increases and the child flourishes. This ill effect is apparently exerted by toxins secreted in the milk, as bacteriological examination of the milk was negative. Waller found that this wasting and vomiting in breast-fed children was due to oral sepsis in the mother in 160 out of 200 cases.

The relationship between focal infection and diseases of the skin, which has been recently reviewed by Dr. H. Leslie Roberts [9], cannot be dealt with here, nor can the relationship of sepsis to certain forms of glycosuria. The endocrine glands are not very susceptible to the influence of focal sepsis. In the course of acute rheumatism the thyroid gland may be enlarged and tender. I have seen exophthalmic goitre develop directly after an attack of acute rheumatism before the patient left the hospital, but this sequence is rare. H. Vincent has, however, observed both exophthalmic goitre and myxœdema as sequels of acute rheumatism. Billings [10] has observed cases of exophthalmic goitre with dental or tonsillar sepsis which rapidly improved on removal of the sepsis. I have seen very few cases of disease of the thyroid gland in which focal sepsis could be regarded as the cause of the malady. In only two of a series of 300 private cases of exophthalmic goitre was such a focus found [11]. In cases of hyperthyroidism and exophthalmic goitre focal sepsis may aggravate the condition or retard recovery. Marked improvement follows removal of sepsis in these cases, but the symptoms do not disappear as one would expect if the sepsis had been the prime cause of the thyroidal disease. The pituitary and supra-renal glands are even less susceptible. Acute pancreatitis may follow oral sepsis, possibly by way of an ascending infection from the bowel. In the present discussion it would carry us too far afield to consider the influence of what may be called systemic, rather than focal, infection in disease, though the modes of exerting such influence are similar to those we are considering.

Under the heading of systemic sepsis may be included infections of the bronchi, bile passages and genito-urinary organs, which may lead to distant lesions, such as gonorrhœal rheumatism. For the same reason the results of the absorption of toxins from the alimentary canal in cases of intestinal stasis is beyond the scope of the present discussion. I should like, however, to mention in passing, that as far as

my own experience goes, the latter condition is much less frequently a cause of disease than has been stated by some writers. In fact, excluding examples of gross organic disease or malformation, I cannot recall a case in which excision of any portion of the bowel was necessary in order to remove a possible source of toxæmia.

The present situation may be briefly summarized by stating that the most frequent sites of focal infection are to be found in the head, in the diverticula of the alimentary canal, and in the genito-urinary organs. The bacteria commonly concerned in these infections are nearly all micrococci: streptococci of various strains, staphylococci, pneumococci and gonococci. To these may be added the colon bacillus and other members of the same group, and, on occasion, various other bacteria may play a part. The maladies which are most likely to result by the direct mechanical conveyance of bacteria from a focal sepsis are infections of the skin, alimentary canal and respiratory passages. Hæmic infection or subinfection and toxins conveyed by the blood may cause septicæmia, malignant endocarditis, secondary and pernicious anæmia, acute and chronic arthritis, neuritis, fibrositis, certain diseases of the skin, and occasionally inflammation of either secretory, incretory, or excretory glands.

REFERENCES.

- [1] ADAMI, J. G., *Brit. Med. Journ.*, Jan. 24, 1914, p. 177. [2] TOPLEY, W. W. C., *Lancet*, July 5, 1919. [3] GODLEE, Sir R. J., *Lancet*, Dec. 5, 1903, p. 1551. [4] WILLCOX, Sir W. H., *Brit. Med. Journ.*, June 4, 1921, p. 805. [5] ROSENOW, *Journ. Amer. Med. Assoc.*, lxx, 1915, p. 1687. [6] HUNTER, W., "Oral Sepsis as a Cause of Disease," 1900 and 1921. [7] ANDREWES, Sir F. W., *Lancet*, Nov. 24, 1906. [8] WALLER, H., *Lancet*, Nov. 4, 1916. [9] ROBERTS, H. LESLIE, *Brit. Journ. of Dermatology and Syphilis*, Nov., 1921. [10] BILLINGS, F., *Journ. Amer. Med. Assoc.*, Sept. 13, 1913, p. 319. [11] MURRAY, G. R., *Brit. Med. Journ.*, Nov. 11, 1922.

Mr. HERBERT TILLEY.

Focal sepsis as it is met with in the throat, nose and ear, has so many and far-reaching possibilities as a factor in disease, that in the preparation of my remarks I have found it necessary to exclude its acute manifestations as well as those which may result from the direct spread of infection into regions in the immediate neighbourhood of the primary focus, so that if one may be allowed to amend the official title in order to meet the limitations of my own contribution, it would read, "Chronic focal sepsis in the throat, nose, and ear, as a factor in disease."

GENERAL CONSIDERATIONS.

The paths by which organisms and their toxins reach their destination may be direct or indirect. From the regions which we are about to consider, the infective elements may be inhaled directly into the lower air-passages and bring about lesions in the larynx, trachea, bronchi and lungs, or be swallowed and cause morbid conditions in the gastro-intestinal tract.

Indirectly, they may travel by the blood-stream or lymphatics and produce a distal manifestation in any organ or tissue of the body—for none would seem to be exempt.

THE THROAT.

Let us consider the faucial tonsils, which are the most frequent foci of sepsis in the throat, and it will save time and repetition if we agree that what is true of those glands applies with equal force to the other constituents of Waldeyer's ring, which includes the lymphoid tissue of the naso-pharynx and the so-called "lingual tonsils."

From a clinical point of view, I regard a septic tonsil one subject to more or less frequent attacks of varying degrees of inflammation and associated with some enlargement of its corresponding cervical gland behind the angle of the jaw.

A further statement would be that the mere size of the tonsils is of little clinical

significance unless, as is often the case in children, they produce symptoms of obstruction. Finally, emphasis would be laid on the fact that small, fibrous, septic and buried tonsils, frequently hidden behind purple-red faucial pillars, are those which are particularly liable to give rise to serious systemic symptoms.

If we put the same question to a pathologist, the answer might be: "A tonsil is of pathological significance when one or more of its crypts contain an excess of polymorphonuclear cells, or when these are found making their way between the epithelial cells which line the crypts." The mere presence of bacteria in those recesses is no evidence of disease, but if and when such organisms pass through the epithelium into the lymphoid follicles of the gland, then morbid conditions may arise productive of local or systemic symptoms. He might also state that the small plugs of epithelial debris which can generally be squeezed from a tonsillar crypt have no pathological significance although they may be of importance in that they provide a suitable medium for bacterial growth. Only when this assumes such a proportion as to destroy the normal epithelium and induces excessive polymorphonuclear migration will the portal be thrown open to invasion of the lymphoid tissue by the organisms and their toxins.

Dr. G. B. Wood, of Philadelphia, from whose work on the subject I am quoting, says it is very important that we should realize the possibility of soluble toxins being absorbed from the tonsil directly into the blood-stream and producing systemic disturbances without a preliminary involvement of the lymph-nodes. The intense septic intoxication which occurs so early in acute tonsillitis can only thus be explained. Bacteria, on the other hand, are probably removed entirely by way of the lymph vessels. Of course, in many instances both channels of infection are open in a varying degree at one and the same time, and the clinical picture will differ in relation to the virulence of the organism and the resistance of the host.

Turning now to the clinical evidence in support of the rôle played by focal sepsis of the throat in disease, I will take a common example familiar to you all, and one which illustrates a mild toxæmia.

In October, 1919, a patient consulted me because of "occasional sore throats and slight feverish attacks." She was easily tired by slight exertion, and an unusual amount of sleep did not refresh her. She was anæmic, the tonsils were septic, and the glands behind the angles of the jaw were enlarged and slightly tender on pressure. The tonsils were enucleated. In December, 1925, the patient wrote to me about another matter and took occasion to say: "I never knew what it was to be really well until you removed my tonsils six years ago."

I think it reasonable to assume that her general symptoms were due to a chronic and mild septic intoxication from the tonsillar foci, and that previous to the operation such a patient would be liable to a more definite manifestation of disease as a result of getting wet through, from an attack of influenza, or from some severe mental or physical shock.

One does not always get such a good result as I have just quoted, and some reasons for this will be offered for your consideration later on.

At the other end of the scale we have examples of the more serious effects of tonsillar sepsis. Poynton, in his lucid contribution to the discussion on "Rheumatic Infection in Childhood" (*British Medical Journal*, October 31, 1925) analysed 1,108 cases of primary attacks of acute rheumatism in children, and states that a great number of these cases developed along the following lines: (1) sore throat, arthritis, and morbus cordis, and (2) those beginning with chorea, and often with morbus cordis also.

Amongst other statements he made are the following:—

"I believe the tonsils to be an important site of infection. I hold that the successful removal of unhealthy tonsils is a valuable prophylactic step if, undeterred by exceptions, we view the problem on broad lines."

At the same meeting Dr. R. W. Miller gave some statistics which strongly supported these views.

While on the subject of heart symptoms I will record a case of chronic tachycardia (120 per min.) in a boy, aged 12, from whom, after a week's rest in bed, septic tonsils were removed. Within ten days the pulse-rate became normal and has remained so for three years.

I have also seen a few cases of chorea which have quickly recovered after enucleation of septic tonsils, but as chorea tends to get well spontaneously, it would not be wise to conclude that my few cases were of the *post ergo propter* order.

Much interest has been directed to the relationship between focal sepsis and arthritis, fibrositis, myositis and other so-called "rheumatic infections." It would be possible to instance many cases in which the earlier types of these affections have been cured by the complete removal of septic tonsils. My friend, Mr. Mollison, of Guy's Hospital, has published his experiences to this same effect.

The most favourable cases seem to be those in which the distal affections appeared at the same time or shortly after an attack of sore throat or tonsillitis, and have been aggravated by subsequent attacks.

PULMONARY SYMPTOMS.

The influence of such infective foci in the production of bronchial catarrh and bronchitis is perhaps most noticeable in children, if we may judge by their frequency and the rapidity with which they often disappear when the chronic foci of infection have been removed from the throat and naso-pharynx.

In later years the cumulative effect of a chronic toxæmia of tonsillar origin seems to produce symptoms suggestive of anaphylaxis, such as vasomotor rhinitis, asthma, urticaria, &c.

GASTRO-INTESTINAL LESIONS.

The swallowing of septic material exuded from the tonsil crypts may be responsible for symptoms referred to the gastro-intestinal tract, but in my experience such distal manifestations are of more frequent occurrence when the focus is of dental or nasal sinus origin. Possibly this may be due to the fact that much larger quantities of pus are discharged from the teeth and nasal sinuses than from the tonsils. Your opinions as to this distinction would be welcome.

Presumably the relatively small amount of material derived from a septic tonsil can be destroyed by the acid gastric juice of a healthy stomach, but we must not depend too much on its bactericidal power, for, as Dr. William Hunter has pointed out, there is a limit to its power of destroying such organisms when they arrive in increased and continuous amounts. Smithies (quoted by Charles Mayo) examined the gastric extracts of 2,406 individuals with "stomach complaints" and showed that irrespective of the acidity of the extracts, bacteria in many forms were present in 87 per cent.

If the organisms escape destruction in the stomach they may infect lower regions in the gastro-intestinal tract, such as the appendix, and thus add supplementary foci of general infection.

This should be borne in mind when removal of a primary focus in the throat or paranasal sinuses has failed to produce a cure or improvement of any distal manifestation, e.g., symptoms of chronic toxæmia, arthritis, neuritis, &c.

OPHTHALMIC DISEASE.

It would be interesting to hear opinions which bear on the relationship between intrinsic lesions of the eye, such as iritis, irido-cyclitis, keratitis punctata, vitreous opacities, &c., and chronic septic tonsillitis. My own experience on this point is too small to be of much value.

RENAL DISEASE.

Of subinfection of the kidney as a sequel of chronic sepsis in the tonsils, paranasal sinuses, or in the ears, I have had little experience, but the association of acute tonsillitis and nephritis is by no means infrequent, although I am not prepared to state whether both are evidences of the same general infection or whether the kidney lesion is in the nature of a tonsillar subinfection.

One must look to the bacteriologists for information as to the organisms responsible for the milder as well as the more severe distal lesions of focal sepsis, and why certain of them appear to have a predilection for particular tissues.

As far as my experience and reading go, the tonsils are an active breeding ground for the *Streptococcus hæmolyticus* and *viridans*, which are found in myositis, arthritic, or cardiac manifestations, while less virulent types are found in the milder forms of general toxæmia.

THE PARANASAL OR ACCESSORY SINUSES OF THE NOSE.

The general considerations which apply to focal sepsis in the tonsil or any other region of the body apply with equal force to the paranasal sinuses. But I would like to make a few statements of a general nature with regard to infection of nasal origin. It is only within the last ten to fifteen years that septic conditions of these air cells have been proved to be by no means infrequent in young children. The symptoms are almost identical with those met with in diseased conditions of tonsils and adenoids, and the removal of these lymphoid structures will cure some 90 per cent. of the co-existing sinus infection without any other local treatment.

But when symptoms such as nasal discharge, obstruction, sneezing, cervical adenitis, anæmia, general lassitude, and mild evening pyrexia persist after removal of tonsils and adenoids, then the physician should insist on a skilled examination (including radiography) of the paranasal sinuses.

In my experience the most frequent distal manifestations of these infections in children are general symptoms of mild toxæmia, a slight and otherwise obscure evening pyrexia, the so-called "growing pains," polyarthritides, bronchial and asthmatic symptoms. In young adults the clinical picture will often resemble that of pulmonary tuberculosis. Of cardiac complications I have seen little, and should like to hear the experience of others on this point.

In adults, and especially when more than one sinus is septic, it is obvious that a large quantity of purulent material will be swallowed in the course of a day if we bear in mind that an average maxillary sinus will hold from 16-18 c.c. of fluid. It is not surprising that indigestion and stomach complaints are more common than in chronic septic tonsillitis. In other instances a general cachexia simulating that of malignant disease may be noticed, and may be regarded as due to toxæmia. I have referred already to the inability of the stomach to deal with a continuous and unlimited amount of swallowed infective material. The entry of this into the lower air passages is a frequent cause of chronic laryngitis, in which there is a particular tendency to irritation and swelling of the interarytenoid fold.

Bronchial catarrh and chronic bronchitis will often find their explanation in a septic accessory nasal sinus.

S. T. Darling¹ is of opinion that lobar pneumonia is often a direct subinfection from such a source, and his post-mortem investigation of the nasal sinuses in a series of fatal cases of pneumonia would seem to substantiate his view. In 91 per cent. of these, old standing pneumococcal infection of the air cells was found!

Until the last year or two one had found little reference in medical literature to the relationship between sinusitis and bronchiectasis. Some evidence of this

¹ *Journ. Amer. Med. Assoc.*, 1906, xlvii, p. 1561.

nexus obtains in a contribution by Dr. James Adam, of Glasgow, and published in the *Journal of Laryngology and Otology*, March 1925. As you are aware, a patient with bronchiectasis is liable to cerebral abscess, and in Eagleton's work on "Brain Abscess" he states that the frontal lobe is most frequently affected. It is, therefore, particularly interesting to note that in Dr. Adam's five cases of bronchiectasis associated with nasal suppuration, two of them died from brain abscess. The natural question we should ask would be: "Is the cerebral lesion due to nasal infection or to pulmonary metastasis?" Perhaps some of you can throw further light on these matters. In any case it is obvious that the obtruding symptoms of bronchiectasis should not lead the physician to forget the possible factor of nasal sepsis.

I have seen a few instances of chronic myocardial lesions quickly relieved by treatment of the nasal sinuses, but cannot recall any instances of acute cardiac involvement which appeared to be of this origin.

It is within the experience of most rhinologists to have seen many cases in which the constant absorption of toxins from the paranasal sinuses has brought about such anaphylactic symptoms as have already been referred to in the case of the tonsils.

The nervous system is peculiarly liable to suffer from the effects of chronic toxæmia. Headache in the supra-orbital, frontal, or occipital regions is an almost constant symptom of sinus affection, and its distribution tends to vary with the particular sinus involved. Migraine and neuralgia of the branches of the second division of the fifth nerve are common in empyema of the maxillary antrum.

Sciatica and peripheral neuritis are frequent results of paranasal sinus infection: As to its baneful effects on the central nervous system and the psychoses the evidence is overwhelming, and I cannot do better than refer you to what has been written on the subject by Dr. Watson-Williams in the Semon Lecture which he delivered last November.¹

ORBITAL COMMUNICATIONS.

The limitation of time prevents me from discussing the relationship between sepsis of the paranasal sinuses and intra-ocular inflammations.

I have frequently heard patients make the voluntary statement that their "eye-sight seems to have improved" after the cure of a sinus infection.

Some seven or eight years ago a man whose life was rendered unbearable by frequent attacks of iritis was referred to me. All the nasal sinuses on the same side were in a state of chronic suppuration. I opened and drained them, and precipitated the most acute attack he had ever had, but he has never been troubled since.

Retrobulbar neuritis as a subinfection from the nasal sinuses was discussed here last month. Ophthalmic surgeons appeared to doubt the relationship, because the tendency of the neuritis is to subside spontaneously or with general treatment. Further observations will be required to settle the question and will demand a closer co-operation between nasal and ophthalmic surgeons.

I must dismiss chronic suppuration of the ear with scant courtesy to such an important subject. Leaving out of the discussion its possible complications with regard to vital structures in its immediate neighbourhood, one can state without hesitation that in the cure of chronic suppurative otorrhea, often one of the pleasing results is the improved general health of the patient; in other words, the removal of a focus productive of general septic intoxication.

Before leaving the subject of the paranasal sinuses, I would ask physicians to suspect these foci, when the patient, with a distal manifestation of infection, states that he has a "post-nasal catarrh," for that is the lay diagnosis of the great majority

¹ *Brit. Med. Journ.*, 1925, ii, p. 916.

of cases of sinus sepsis which come before the nasal surgeons. To the patient the arthritis, neuritis, indigestion, or other troubles are the source of anxiety, and often no mention is made of, and no question asked as to symptoms referable to the upper air passages.

From such disjointed observations as I have brought before you, the need for early detection and removal of foci of sepsis will be obvious.

But prevention is better than cure, and to this end we shall all be in agreement that the Education Act of 1921 is one of the greatest pieces of social legislation ever enacted. For it makes it the duty of municipal authorities to give skilled care and attention to the health of children in the Council Schools. So that in so far as diseases of the teeth, throat and upper air passages are concerned, a large area liable to foci of infection should be under frequent supervision. It is impossible to over-estimate what this may mean in the prevention of maimed hearts, crippled limbs, deafness, and chronic suppurative otorrhœa with its attendant and serious complications.

In what has been said as to the rôle played by septic foci in the throat, nose and ear, I hope that you will not blame me if the views expressed appear to be too dogmatic. With a time-limit restriction, bare statements have to be made which often contain only half truths.

In conclusion, I will state how the whole question appears to me. We have an overwhelming mass of evidence which proves that focal sepsis is a factor—possibly the predominant factor—in certain diseases and that the nidus of infection should be completely removed as the first item in treatment unless there are considerations which demand delay. At the least such treatment will remove one burden from those organs and tissues the function of which it is to combat infective organisms and their toxins. On the other hand, we all know that some distal manifestations of a focal sepsis disappear not only when the source of infection remains untouched, but even when no treatment of any kind, local or general, has been accorded them.

An equally and perhaps more frequent experience is that only a partial improvement follows removal of the primary focus. This is sometimes due to the fact that others have been overlooked, e.g. in a case of arthritis suppuration in one or more of the nasal sinuses may be cured, but a gastro-intestinal, gall-bladder, appendix, prostate, or utero-vaginal source of sepsis may remain. Even in the absence of such secondary sources the removal of the primary focus may fail to do more than relieve a distal subinfection until the diet of the patient is carefully regulated, or massage, change of air, a sun cure, spa treatment, or even endocrine therapy, may quickly bring about further improvement or perhaps a cure.

Finally, there remain those cases which progress from bad to worse in spite of any or every form of treatment, and we can only stand by and relieve symptoms as they arise. Surely such experiences prove that even if we regard focal sepsis as a predominant factor in certain diseases, it is not the only one on which we should rivet our attention.

If this view be correct one deduction is obvious, viz., the need of a closer co-operation between physicians, surgeons, specialists, biochemists, bacteriologists, and pathologists—in fact all who by their training and experience can add to the common knowledge of disease processes as they affect the human being, that most complicated mechanism in this most wonderful world.

Mr. F. W. BRODERICK (Bournemouth).

I am asked to deal with this matter from the standpoint of dental sepsis, but I think that several of the points that I wish to raise will be applicable to chronic sepsis in other parts of the body.

The most noticeable thing from the point of view of the practising dentist,

especially one who studies any number of radiographs, is the extraordinary number of patients who show signs of periapical absorption with presumably no symptoms of general infection, persons who are, notwithstanding this condition, in perfect health.

On the other hand one cannot fail to be struck by the enormous improvement that does occasionally take place on the removal of infected teeth in certain cases referred to us by medical practitioners. Further, it is not necessarily in those cases in which the sepsis would seem to be greatest that symptoms of general involvement always show themselves; extensive destruction of alveolar tissue, and large areas of periapical rarefaction, may exist with perfect health, whereas small, insignificant foci may be the cause of extensive degenerative changes.

The explanation of these facts cannot lie altogether in the question of the bacteriology of the infection, rather will it be found in the resistance of the body to those infections, and the study of the individual's defensive power should give us a clue, not only to the danger of the infection, but also to its treatment. Modern physiological teaching shows that the defensive powers of the body are mobilized and maintained by the autonomic nervous system, controlling and controlled by the endocrine apparatus; that the two portions of this, the sympathetic and the parasympathetic, are antagonistic, and that a correct balance between the two parts is necessary to health.

Under ordinary circumstances the reaction to infection will show itself by an increased metabolism, bringing an increased blood-supply to the part, followed by a leucocytosis; if this reaction is sufficient, the parts will return to normal, if insufficient, suppuration will take place with abscess formation. Where, however, we find chronic sepsis, neither of these ends has been attained, or only to a very limited extent.

With the periapical infection that we are now considering, it is rare for the onset to be accompanied by noticeable symptoms of sympathetic stimulation, and discomfort is rarely present.

Vines, in explanation of the rationale of the treatment of chronic ulceration with parathyroid extract, calls attention to the fact that whereas the thyroid and the suprarenal act as stimulators of the sympathetic, there is a probability that the parathyroid stimulates the parasympathetic; that whereas the former produces the initial metabolic increase, the latter produces the leucocytosis, and that if the reaction of the former is not balanced by that of the latter, infections tend to become chronic. If we consider those cases in which a chronic septic focus has caused a general systemic infection, we shall see that the results, in many cases, point to an endocrine or a nervous cause.

Let us take arthritis as an example. In reading the discussion on the ætiology of this disease that took place at the Bath meeting of the British Medical Association last summer, one finds opinion about equally divided between an infective focus and an upset in metabolism being the chief factor. I did not notice, however, that any speaker connected these two together in any way. Looking at the question of chronic infection in the way that I have suggested surely one can see that there is such a connexion.

Pemberton reports that the only common factor in a large number of cases of arthritis he studied was a lessening of sugar tolerance, and that under treatment these improved whether the septic focus, if present, was removed or not. Thompson definitely divides these cases as to whether they show symptoms of hypo- or hyperthyroidism, and Llewellyn Jones Llewellyn traces the pathology of all the rheumatic diseases to an upset in the endocrine autonomic balance.

Several speakers at Bath stressed the factor of anxiety and grief as important predisposing causes, which, from the work of Cannon and of Crile, we now know to produce their effects through a suprarenal over-stimulation, and an upset balance

between vagus and sympathetic. If, then, an important factor in the production of chronic sepsis is, as I have suggested, a similar upset, we can reconcile the two ideas and get a step nearer to the aetiology of a number of diseases, going one step further back behind the condemned focus.

Thinking on these lines, we see that the chronic infection is not the cause of the arthritis—rather the infection and the arthritis are caused by the same thing. Still, it is necessary to remember that the chronic sepsis once existing, this may further depress the autonomic nervous system, preparing the way for other troubles, and that by the time that the diagnosis is made we may be in the grip of a vicious circle, which may best be broken at the tooth or tonsil point.

DENTAL SEPSIS.

Coming more directly to dental foci, we find conditions present that are exceptionally favourable to chronic sepsis. A tooth in which the pulp has been destroyed, and which contains an infected pulp chamber, is a very difficult problem from the point of view of body defence, since it is impossible, however well the blood may be circumstanced to overcome that infection, for it to bring all its advantages to bear. The micro-organisms entrenched within the tooth are able to draw their sustenance by way of the lymphatics in the periodontal membrane, through the root tissue, while they themselves remain there inviolable and protected from the blood-stream. The only place at which the defensive powers of the body are able to attack them is at the root apex, at which point they issue forth through the dental foramen, and here the body attempts to produce a quarantine barrier in the form of the so-called granuloma. Now it so happens that the very presence of this granuloma, recognized by an area of rarefaction at this spot, is as a rule sufficient, in the minds of most men, to condemn the tooth, as being in itself a proof of infection, whereas in reality it shows the reaction of the body to the infection, and in many cases a very satisfactory reaction.

Weston Price, of Cleveland, U.S.A., whose work on chronic dental foci has been very elaborate and extensive, explains that those patients who exhibit granulomatous formation at the roots of so-called dead teeth, together with areas of bony rarefaction, are in every case those who do not present symptoms of general systemic involvement; whereas where there is a dental infection without granuloma and without rarefaction of alveolar bone, but with a tendency rather to hypercalcification, there is invariably some systemic derangement. This statement, however, requires this qualification, that it is possible, with what Price calls an overload, for the quarantine thus set up to be broken down; under these circumstances the bone surrounding the granuloma tends to condense and the vascularization to diminish. Price has also shown that the granulomatous tissue is sterile and bactericidal, and that teeth protected in this way placed beneath the skin of rabbits protect those animals from general infection.

On the basis of extensive clinical observation, Price divides patients showing local evidence of dental infection into three groups: (1) those immune to rheumatic complications, who are able adequately to deal with the infection by the formation of a granuloma; (2) those susceptible who are unable to do so; and (3) those with an acquired susceptibility through overload, in whom the defences set up against the infection have broken down. He also points out that patients in the immune group show, on blood examination, a high ionic-calcium index, a high blood-sugar together with a leucocytosis, this proving that they are capable of dealing with the infection, whereas in the susceptible individuals, the ionic calcium and blood-sugar are low, and the polymorphonuclear leucocytes diminished. Also, in a large number of cases that have been watched, where immunity has broken down under strain, the blood changes pass from the one extreme to the other, as the bone changes progress. This is

interesting in that it upholds Vines' findings that healing tends to take place when the blood-calcium returns to normal, and that this is accompanied by a leucocytosis.

Another method of approach to the problem before us, which will lead, I think, to the same conclusion, is that a large number of us do not now believe that the dental conditions that must of necessity have preceded the chronic sepsis, caries and pyorrhœa, are essentially local conditions at all, but rather themselves the result of general systemic upset.

I believe that the predisposing cause of caries, without which stagnation and fermentation of food can have no effect, is an alteration in the acid base balance of the blood towards the acid side. This may be brought about by a variety of conditions, amongst which endocrine instability is probably the most important. Under these circumstances, calcium salts, normally used for tooth hypercalcification after eruption, are required and utilized for neutralization purposes, in place of less precious alkalies, and in more extreme cases the lime-salts of the teeth themselves may be commandeered for that purpose. It is this very condition which, according to Dr. Llewellyn, constitutes the basis of the rheumatic diathesis; he describes these patients as "living on the edge of an acidosis."

Pyorrhœa, on the other hand, I believe to be brought about as the result of an attempt to compensate an alkalosis, by the excretion of large excess of alkali, when the lime-salts normally excreted by the saliva are greatly increased in amount, and cause the deposition of that hard, dark, subgingival tartar around the necks of the teeth. This tartar acting as an irritant lays the part open to infection, pocket formation and alveolar destruction.

Now Price explains that the infection produced by pyorrhœa does not, except in cases of overload, tend to give rise to general involvement; indeed, he maintains that these cases are immune from rheumatic conditions, so long as the pyorrhœa or the condition that causes it remains active.

Mr. Graves, Medical Superintendent of the Rubery Hill Mental Hospital, showed me some time ago a large number of histories of patients in his institution treated for mental instability by removal of chronic foci, together with intramuscular injections of calcium chloride, with extraordinarily good results. Here it would seem that the focal infections had acted as an overload to the unstable emotional conditions. And as showing the result on the defensive mechanism of the body, it is interesting to record that in a number of his cases, as also in those of Vines, treated with parathyroid extract, the chronic infection lighted up an acute one, with the formation of pus, which is a proof, at any rate, of an increased attempt on the part of the body to deal with the invaders, even if this attempt be not successful.

Regarding the matter from this standpoint, we see that focal infection may or may not be a factor in the ætiology of disease. The result depending not on the infection, its source, or its position, but rather on the reaction of the body to that infection, we see that this reaction is a matter of stability and balance of the endocrine autonomic system, and that this stability depends on heredity and overload.

We have here an explanation of that otherwise inexplicable fact that these dental foci can exist in such enormous numbers without producing any bad effects at all, whereas they may, on occasion, cause serious disease elsewhere; we have an explanation also of the common experience that the removal of infected teeth is so often a disappointment, and of what has seemed the most extraordinary paradox, that the most extensive infection is often the least dangerous.

In addition, we are now able to differentiate between those teeth that constitute a danger and those that do not; this to me, as a practising dental surgeon, seems to be the most important gain of all. For I would stress most particularly the value of some natural teeth, especially in those patients to whom nourishment means so much. Whilst agreeing that there are times when extensive extraction of teeth

is a necessary and essential part of treatment, I would plead that the case of each tooth be considered separately, and that the sound teeth be not sacrificed with the diseased, and that if one, two, or three healthy teeth be found within the mouth the natural denture be not wholly destroyed.

Anyone who has undergone the anxiety and distress of attempting to supply comfortable and serviceable artificial masticating substitutes to some of those patients who have been ruthlessly robbed of their own teeth, so often with little or no benefit to their condition, will realize that to their original indisposition has been added another, and often more serious, complaint, and that rather than benefiting by the surgical procedure, their unhappiness has thereby been very greatly increased. Natural teeth have a value, and a halt should be called to the present fashion of wholesale extraction as a shot in the dark.

Dr. F. G. THOMSON (Bath).

I propose to confine the few remarks I shall make to the influence of focal infection in the causation of arthritis. In the case of so-called rheumatoid arthritis, I am so deeply impressed by the importance of focal infection that I suggest that the somewhat misleading name, "rheumatoid arthritis," should be deleted entirely from the nomenclature of disease, and the term "focal arthritis" be substituted. The name "focal arthritis" not only draws attention to the presence of some underlying infective focus, but emphasizes the fact that it is the duty of the medical attendant to discover where that focus is and deal with it radically and effectively at the earliest possible moment.

No reasonable person will contest the fact that gonorrhœal arthritis is the direct result of infection by the gonococcus, and if you take a series of cases of gonococcal arthritis, and of multiple arthritis in which no suspicion of venereal infection exists, the actual joint lesions will be found essentially alike in both series—so much so that in most cases it is impossible to distinguish between them. It is therefore a fair logical inference that if one series is due to infection by the gonococcus, the other is due to infection by some other organism. Now, in rheumatoid or focal arthritis gross infective lesions either of the teeth or tonsils are found in about 75 per cent. or more of cases, and in many others it is possible to demonstrate definite infection of the intestinal or urinary tract. The mere presence of a focal infection, coincident with a condition such as multiple arthritis, is no evidence that the two conditions stand in the relationship of cause and effect, but when the complete and early removal of the infective focus causes rapid abatement, or even a complete cessation of the articular symptoms, the inference is, I think, fairly obvious, that the arthritis was of infective origin. When one is fortunate enough to see a case of multiple arthritis, with a definite local infection in its earliest stages, it is remarkable to see how the joint symptoms disappear simply and solely as the result of adequate treatment of the focus of infection. One has seen this happen in a number of cases when the infection has been in the teeth, tonsils, or urinary tract. Unfortunately valuable time is often lost in futile attempts to treat the disease by anti-rheumatic or other drugs before the *fons et origo mali* is located and treated. Attempts to isolate specific organisms from the synovial fluid and joint tissues have been generally unsuccessful, and it is doubtful whether the arthritis is due to the organisms themselves or to their toxins.

Though chronic infection of the teeth, tonsils, urinary tract or other organs and regions is almost universally common, only a small proportion of cases develop multiple arthritis, and it would appear that there must be some factor other than infection required to determine the onset of inflammatory changes in the joints. Whether this factor is connected with want of endocrine balance or with other biochemical anomalies is a matter of conjecture, but there is one significant fact which

may exercise a bearing on the case, and that is that all or nearly all cases of multiple arthritis show a complete absence, or a much diminished percentage, of hydrochloric acid in the gastric juice.

The absolute or relative achlorhydria probably acts by the permitting of secondary intestinal infection. Organisms which gain entrance to the stomach from dental or faucial infection are normally destroyed or inhibited in the acid medium of the gastric juice. In achlorhydria they gain access in greater numbers, and in a more active state, to the alkaline medium of the small intestine, which is eminently favourable to their growth, and in which they multiply exceedingly, more particularly if there is any degree of intestinal stasis present. The presence of secondary intestinal infection probably accounts for the unsuccessful results which follow dental extractions or tonsillectomy in cases which are not treated in the earliest stages.

Turning to the other great group of chronic arthritis, viz., hypertrophic or osteo-arthritis, as exemplified by the senile hip, focal infection appears to exercise little or no influence whatever. Osteo-arthritis is a purely degenerative condition, associated with arterio-sclerosis and malnutrition of the joint, the actual determining factor being injury or strain. It is quite possible that the osteo-arthritic joint may become secondarily infected by organisms of very attenuated toxicity. Such a proposition is very difficult either to prove or disprove, but in any case focal infection plays a very subsidiary and unimportant role in the history of the disease.

Mr. T. C. GRAVES (Birmingham).

FOCAL SEPSIS AS A FACTOR IN THE CAUSATION OF MENTAL DISORDER.

Whilst observing the effect of the administration of calcium on the circulatory disturbances associated with mental disorders I noted [1] that in some cases there was a coincidence in the improvement affecting the circulatory and mental states with the development of a more active purulent reaction around septic foci, and removal of these foci was followed by a greater stability of the circulatory and mental states [2]. These observations correlated the work of Grove and Vines, of Cambridge [3], and of Henry A. Cotton, of Trenton, New Jersey [4].

Time does not permit of a lengthy examination of the many aspects of this problem. I will, however, offer some evidence on the subject by means of lantern slides illustrating some types of septic foci found in the mentally disordered and a few photographs of cases showing results of treatment.

(1) *Does focal sepsis exist in association with mental disorder?*

(1) The usual periapical rarefaction around the apex of a crowned and root-filled tooth in a non-certified case of acute depression. Full recovery followed the removal of this and other infected teeth.

(2) The growth of a similar area of rarefaction around the apex of a stump. This second film was taken a year later than the first, and shows that the rarefaction has become larger—from a case of delusional psychosis.

(3) A large dental infected cyst around the apex of a stump.

(4) Shows more infected stumps with areas of bony rarefaction around them—from a case of depression and continued confusion, with an absence of free hydrochloric acid in the gastric juice.

(5) Areas of rarefaction in the upper jaw around the roots of teeth where crowns had been shorn off in order that a denture could be fitted over them—from a case of melancholia.

(6) An abscess extending into the bone around the root of a stump, together with other areas of rarefaction around stumps—a case of confusion with excitement; the patient improved after dental treatment and was discharged.

(7) A series of roots with areas of bony rarefaction around them.

(8) The same in closer detail from a case of apparent dementia in a woman, but showing improvement following their removal.

- (9) Similar rarefaction areas in the jaws—from another case of depression.
- (10) An area of rarefaction around the roots of a carious molar—from a case of confusion.
- (11) Pyorrhœic change in the bone from a case of myxœdematous psychosis.
- (12) A further development of the pyorrhœic process around the teeth of a man, the subject of grandiose delusional psychosis. Following removal of these he recovered and was discharged.
- (13) The lower incisors of a man the subject of uncertified acute melancholia with suicidal intent and ideas of unworthiness, which disappeared after removal of the affected tooth. The film shows the complete isolation of the incisor by the pyorrhœic process.
- (14) Two molar teeth with areas of rarefaction extending down into the bone to the inferior dental canal—from two cases of mental disorder.
- (15) Complete isolation of a solitary incisor tooth, the ulcerative process extending deeply into the upper jaw, and on the same side an infected antrum containing flocculent fetid pus of mixed bacteriology, part of a pansinusitis and ethmoiditis—from a case of myxœdematous psychosis with delusions of poisoning, &c.
- (16) Section of the thyroid of the same case—no acini are to be seen.
- (17) The condition of the mouth of a woman of 70 admitted in a state of confusion and extreme ill-health. Following the removal of the teeth she recovered, even at that age, and was discharged.
- (18) The fauces of a woman the subject of depression. The tonsils are enlarged and infected, and the posterior pillars are swollen with œdema.

These films and photographs have been submitted as a few of the types of the conditions found in oral and nasal sepsis met with in cases of mental disorder. For further information I would refer you to psychiatric literature and the report of the Board of Control for 1924.

(II) The next question is, "*What is the effect of surgical treatment of these foci?*" Interference with chronic septic foci may have two effects. The general and mental condition may become worse or better.

(a) *The Exacerbation Reaction*, if it occurs, becomes manifest within a few days of interference, and its duration and intensity are variable, dependent on the extent of the interference, the nature, duration and extent of the septic process and the resistance of the patient. As a general rule the exacerbation reaction is usually followed by an improvement which brings the patient to a much healthier mental and physical state than before the interference.

It is this exacerbation reaction which is responsible for the development of psychotic symptoms following surgical and dental interference in some patients who before operative measures are regarded as sane, e.g., following dental extraction, occasionally appendicitis operations and puerperal conditions.

(b) *The Improvement Reaction*.—Dependent again on the nature, duration and extent of the chronic septic process, the development of degenerative processes and the resistance of the patient, the elimination of chronic septic foci may result in an improvement which as a rule is not manifested until some appreciable time has elapsed and sometimes may not be definitely noted even until a year or more has passed.

I will now show some photographs from untouched negatives illustrating improvement following treatment of septic conditions.

(1) The first photograph shows the depressed facial appearance of a young married woman the subject of melancholia. Three carious teeth and a buried root were removed and some uterine endocervicitis treated.

The next photograph taken about three weeks later shows an improved facial appearance and the next one a fortnight later a still happier facial aspect. Catamenia, which had been in abeyance, returned. She was discharged recovered, having gained a stone in weight during about six weeks. Note the narrowing of the palpebral fissure on the same side as the carious teeth in the first photograph and its gradual diminution as shown in the later pictures.

(2) This set of photographs illustrates the improvement in a case of mania. The first

photograph is dated April 9, 1924, and the second May 7, 1924. The first shows instability, the second stability. In this case septic roots, carious and pyorrhœic teeth were removed soon after the first photograph was taken.

(3) The following series illustrates the improvement in a case of confusion and encephalitis lethargica following the gradual removal of seventeen septic roots and carious teeth and the copious administration of calcium by mouth and injection.

Admitted on June 12, 1925, he was confused, noisy, threatening towards the staff of the hospital where he had been previously under treatment, deluded in many ways, e.g., imagined he had cancer of the throat, that there was poison in his water. He was also the subject of auditory and visual hallucinations.

The first photograph, dated June 27, shows bilateral ptosis and a squint of the left eye—weakness of the external rectus—and the expressionless face.

The next photograph, dated July 20, shows the expressionless facies, bilateral ptosis still present; the squint has gone but the sclerotics are plainly visible beneath the cornea.

The next photograph, taken on August 7, shows more facial expression but the bilateral ptosis is still obvious.

The last photograph, dated October 5, is a complete contrast to the first. The ptosis is not noticeable and the facial expression is much more normal. The improvement shown facially was associated with a mental recovery.

On admission he weighed 6 st. 12 lb.; on discharge, 8 st. 5 lb., in October, 1925. Since then improvement has been maintained, he is back at work and weighs 9 st. 8 lb.

(4) The next series of photographs illustrates the improvement in a case of confusion with grandiose delusions in a girl of 17.

The first picture shows the condition on admission; the second following medicinal treatment shows her much improved but the subject of pathological mischievousness. The third, after operation by Mr. F. D. Marsh, for removal of septic tonsils and adenoids, a more sober facial appearance and a diminution in the size of the goitre easily visible in the second picture.

The next pair of photographs shows the improvement in appearance of a case of confusion with grandiose ideation following removal of septic tonsils by Mr. F. D. Marsh.

The next pair of pictures illustrates the improvement in a case following treatment of oral and tonsillar sepsis in a girl the subject of delusional psychosis. She recovered.

These are only a few examples illustrating the relation of chronic septic infection to mental and emotional disorders, and I am convinced that these chronic infective processes play a great part in the production of these disturbances.

REFERENCES.

- [1] GRAVES, T. C., "Colloidal Calcium in Malnutrition, Chronic Sepsis and Emotional Disturbance," *Lancet*, 1922, ii, p. 957. *Ibid.*, "The Relation of Chronic Sepsis to so-called Functional Mental Disorder," *Journ. Ment. Sci.*, October, 1923; and "The Incidence of Chronic Infective Processes in Mental Disorder," *Journ. Ment. Sci.*, October, 1925. [2] VINES, H. W. C., "The Rationale of Parathyroid Therapy," *Brit. Med. Journ.*, 1923, ii, p. 854, &c. [3] COTTON, HENRY A., "The Relation of Chronic Sepsis to so-called Functional Mental Disorder," *Journ. Ment. Sci.*, October, 1923 (gives an extensive bibliography).

Mr. G. A. PEAKE (Cheltenham).

I have had, amongst others, some few very interesting cases of mouth sepsis that are worth a passing note:—

Some twenty years ago a lady of good social position had what was then known as "Riggs's disease of the gums." It would now be recognized as an advanced and neglected pyorrhœa. Her teeth were all loose, especially the upper and lower incisors, covered with calculus, and her breath was very foul. She would not hear of artificial teeth because her "mother had never worn any." So I was not allowed to do anything except remove the calculus at intervals. One or two years after she first came to me pus began to form round the left upper central, which was quite free from caries. After the pus had begun to accumulate the pulp of this tooth died, with the usual pain (she refused extraction); this was followed by acute swelling, which rapidly extended up the left side of the nose. She complained of seeing dark spots on everything she looked at unless she covered the left eye. I sent her to an oculist;

neither he nor I could induce her to have the tooth extracted. Three days later the left eye suppurated and had to be enucleated. Her subsequent history is interesting. She has never had a tooth extracted, but they have all fallen out from alveolar absorption. Her age is now over 80 and she is wonderfully well.

Within ten days of seeing the foregoing case there occurred that of a hospital patient, aged between 30 and 40, with an acute swelling and abscess round the same tooth, i.e., the left upper central, also extending up the left side of the nose. The infiltration was so brawny that I took her into the hospital. I removed the tooth and made a free opening into the abscess. The left eye suppurated and had to be removed. I lost sight of this patient, so do not know her subsequent history.

These are the only two cases of that sort that I have come across, and it is curious that they occurred within ten days of each other.

A group of four cases; one of these is remarkable.

A lady, aged about 49, single. Had been a patient of mine for many years. Her mouth would now be recognized as septic, but, according to the extent of my knowledge at that time, it was clean, with much alveolar absorption and so-called gum retraction. She was entering for an appointment that necessitated a medical certificate. The physician who had to pass her for this was a very able man and well known for his thoroughness. He made, so he told me later, the usual examination of everything, and passed her as A1. Quite shortly after this, before the appointment was settled, two lower premolars left, with no caries, became inflamed. An appointment was made to extract them, but was not kept, for the evening previous to the appointment she complained of sleepiness and rapidly became comatose. Her medical attendant was sent for; he obtained a specimen of her urine and found a heavy percentage of sugar. She died the next day. Post mortem nothing abnormal was found in any organ. In this case one seems to have witnessed the onset of the diabetes, and there was apparently no cause except the septic mouth.

The other three patients were all men—an army man and two who have never had to work. They were recognized diabetics when sent to me—all with very septic mouths which I cleansed, but I understand the sugar percentage has not decreased in any one of them.

One other curious case. A retired Army major; year 1919. Of fine physique and a very good cricketer. His right arm "began to tingle and after a short time it was getting numb," and in three to four weeks he could not voluntarily move it. He saw several specialists, who told me they were nonplussed. Wassermann reaction carried out several times: always negative. His teeth were free from caries, and the few fillings had been carefully executed. His mouth was clean, except for slight loss of alveolus and gum retraction. In this year, 1919, I was a great believer in extraction, and I took out all his teeth. In five to six months all power had returned to his arm, and one year after the extractions he was able to bowl again and got quite a good average. I saw him a few weeks back; he is still grateful to me, but I often wonder whether with the very slight physical signs in his mouth I was right in extracting all those teeth.

I have had other cases of moderate success, of course. But on the other hand I have had a very large number of acute disappointments. Patients have been sent to me for (1) joint and muscle pains, (2) malaise, (3) dyspepsia, (4) eye troubles, (5) ear troubles, (6) jaundice, (7) stomach troubles—suspected ulcers, and ? malignant disease.

For some years I have treated them by extraction of their teeth, and though the state of many of these patients has appeared for a time to have improved, I am unable to claim that three years after clearance of their mouths they were absolutely cured of the troubles with which they came to me, and a good proportion of them are worse. The stomach cases have certainly shown better results than the joint and muscle cases.

Dr. Townsend, superintendent of a private home for mental patients in Gloucestershire, tells me that for some years past he has made it a rule, whenever he could obtain permission from the relatives, to ensure that the patient has a clean mouth as

early as possible after admission. His experience is that of all these patients dentally treated very few, if any, showed more improvement than those not treated, and also that he has been unable to trace any connexion between mouth sepsis and mental disorders. This is disappointing.

Against this he has had at least one good case. The patient was a man who became suddenly suicidal. He was also a personal friend of mine and for ten years at least he had had a very filthy mouth which he would not have treated. When he went to the mental home I obtained permission to clear his mouth and fit dentures—after about eighteen months he recovered and went back to his work.

Bearing in mind these and other cases I have dealt with, my own mind is not at all settled as to how far dental and mouth sepsis is responsible for all the faults attributed to it. I am certainly convinced, from my many failures, that wholesale extraction on the slightest sign of sepsis can be carried too far. There are of course a large number of cases in which total extraction is the only correct and possible treatment, but again there are many cases (I see them daily all round me) which are treated by extraction, when I think the patient would be far better equipped to fight his own medical troubles by having the very superior mastication of his own teeth, allowing the patient's own internal economy to deal with the slight sepsis that will still continue.

Possibly we dentists are not without blame. We have no consensus of opinion on this matter. Some see pyorrhœa when there is only a simple gingivitis; some do not see pyorrhœa when to me the mouth is filthy. Some are apparently swayed by the patient who has culled his knowledge from the press; some are urged forward by enthusiastic X-ray specialists; some by medical confrères who send their patients on to us with "instructions" to have all their teeth out. This may not be so in London, but it is very much so in the country, and the result to-day is a massacre of teeth that "out-Herods Herod."

Dental surgeons should ask themselves "Quo vadis?" Are we going to be "extractors and adaptors," led by a foremost London dental surgeon, who, so far as I can make out, strongly advocates extraction in every case; or, shall we do all we can to preserve patients' teeth and keep them away from the indifferent mastication of dentures, at least until such time that mastication is not of such great value to them? If the latter course, I would suggest to those responsible for the recent recruits to the dental profession to see to it that men have, when they start practice, something far better than the simple armamentarium they bring to-day, namely, prescriptions for saline mouth-washes, followed by X-ray photographs, then forceps, then dentures. This for every patient.

Dr. E. STOLKIND.

My remarks will only refer to the relation between infected teeth and general diseases and to the irrational extraction of teeth.

A large number of practitioners now attribute nearly one-third of all diseases, internal, nervous, mental, ocular and others, to focal infection from the teeth and gums. This conclusion was based in the first instance on some clinical observations and more recently on some bacteriological researches.

Streptococci, staphylococci and other bacteria were cultivated from the pus and alveolar abscesses, and the infected pulp of the teeth; and from the pus in cases of alveolar pyorrhœa. During the last twelve years Rosenow, and later Billings, Haden, Price and others, after performing experiments on lower animals came to the conclusion that there are marked evidences of specific elective-tissue affinity from the pathogenic streptococci from the various tissues and likewise of the primary foci. This discovery and the production of a similar infective process in the lower animals,

mostly rabbits, when inoculated from the tissues from which the bacteria are afterwards recovered, constitute, in their opinion, proof of the ætiological relation of the focus of infection to the systemic disease. Rosenow and Meisser produced urinary calculi or lesions of the medulla of the kidneys in 87 per cent. of the dogs whose teeth were infected with streptococci from the urine, infected teeth and tonsils of nine patients with typical nephrolithiasis. These very interesting experimental researches have so far not been confirmed by other bacteriologists.

An experimental study carried out by Haden (in 1924), in which over one thousand root tips were cultured by a quantitative technique, revealed the fact that 40 per cent. of the pulpless teeth, which are shown to be negative in the radiograph, harbour a sufficient number of bacteria, to render them a possible factor in systemic disease.

Some clinical observations, and partly these experimental researches, had led a great number of doctors to believe that there is a close relation between dental defects and general diseases. As a consequence of the belief in the close relation between dental defects and general diseases, in nearly every case of obscure pathology, especially if it is a difficult one for treatment, the teeth, sometimes the tonsils, adenoids, and more rarely other local foci, are regarded as the causative factor of the disease. Generally in such cases the medical advice is to have all teeth extracted.

During the last ten years I have had under my observation hundreds of patients who, upon the advice of their medical attendants, have undergone extraction of all their teeth. Others before accepting the advice to have all their teeth out have consulted me. I will mention only a few of these cases.

My first such patient was a woman suffering from trigeminal neuralgia who was advised by several doctors to have all her teeth extracted. The dentist at first took out only three teeth which proved to be in good condition. The pain continued. Besides neuralgia the patient was suffering from gout. Diet, arsenic, hydrotherapy, &c., relieved the pain and no more teeth were extracted.

Later, I saw many other cases of trigeminal neuralgia in which physicians had acted according to their fixed idea, i.e., that it is caused by bad teeth. About 70 per cent. of my patients suffering from neuralgia had undergone extraction of all their teeth without any relief resulting. The same holds good of many patients suffering from other nervous diseases. In the out-patient department I have seen large numbers of cases of neuritis, perineuritis, neuralgia, neurasthenia, psycho-neurosis, disseminated sclerosis, even tabes, progressive paralysis, Graves' disease, paralysis agitans, muscular atrophy, cases of sequelæ of epidemic encephalitis, &c., in which all the teeth were extracted without any beneficial result. Many patients suffering from headaches and migraine had had all their teeth taken out, whereas these troubles were really due to disturbances of the eyes, or in the sinuses or to anæmia, &c.

It is quite usual to see patients with "arthritis" who, upon medical advice, have had all their teeth extracted without any improvement. Since, in my opinion, the cause of arthritis is not dental infection, many patients of mine with arthritis, without having their teeth out, have improved under non-specific protein therapy, diet, hydrotherapy, &c. Ashcroft, Cunningham, McMurray and Pemberton, by investigation of fifty cases of arthritis deformans, have isolated a new organism, have found diminution of carbohydrate tolerance and have obtained improvement without the removal of focal sepsis.

All the teeth were removed in some of my patients suffering from angina pectoris, asthma, diseases of the stomach (especially in cases of gastric ulcer), intestines, liver, also in some cases of pulmonary tuberculosis with pain in the chest, &c. Generally the patients felt worse after the extraction.

The following are some instances:—

A woman, aged 50, was suffering for a year from frequent asthmatic attacks, dyspeptic symptoms, neurasthenia, &c. She was told by her doctor to have all her teeth out, on the

ground that her illness was caused by them. The dentist had found only a few decayed teeth, but on the instructions of the doctor he took out the good teeth as well as those decayed. The attacks became worse. An abdominal belt, diet, hydrotherapy, iodine, &c., very much relieved the patient; there were no more attacks for the following six months, and few after that period.

In another case, a male patient, aged 37, with psychoneurosis and some pain in the right side of the abdomen, was advised by three physicians to have all his teeth out; this was done in October, 1924. Since then he became much worse. He did not "enjoy his food," he lost his appetite, became weaker and more nervous, and was unable to follow his occupation.

I have under observation many patients suffering from various diseases who were advised by other physicians, on account of their general state of health, to have all their teeth extracted.

For instance, a male patient, aged 45, consulted me in April, 1920. He complained of weakness of the legs and nervousness. A physician told him that all the teeth should be extracted, since they were the cause of his ill-health. He has so far retained all his teeth, and his general health has improved.

In another case a London doctor with dyspepsia was advised by a physician to have all the teeth extracted, since they were the cause of his illness. At first only some of them were taken out. After the operation the patient became very weak; I saw him when he recovered. In my opinion the extraction was unnecessary.

Another patient with stenocardia and true alveolar pyorrhœa was advised by me to have his teeth thoroughly treated by scaling, massage of the gums, cleaning, tightening of the loose teeth, &c., but not to have them extracted except in case of alveolar abscess, &c. Under a restricted diet, &c., the patient has so far felt much better.

In my opinion the relation of the teeth to general diseases is greatly exaggerated, not only by the dentists but also by the doctors. Besides, even the diagnosis of alveolar pyorrhœa is often incorrect.

I have seen many cases in which alveolar pyorrhœa was diagnosed and the extraction of all the teeth advised, and in which only carious teeth, tartar, alveolar atrophy or gingivitis were found. Purulent gingivitis is often mistaken for alveolar pyorrhœa. In some cases the gingivitis was caused by diabetes mellitus. Even in cases of alveolar pyorrhœa all the teeth, or at any rate the majority of them, can be saved by proper treatment. Only when there is alveolar abscess, or when the tooth no longer functions as such, is it advisable to take out the particular tooth. Often it was necessary to remove only one or two teeth.

Owing to a wrong diagnosis of the ætiological factor and irrational treatment, millions of healthy teeth have been unnecessarily extracted, and in the out-patient department toothless mouths, especially in people of the working classes, are very common phenomena constituting a public danger so far not sufficiently recognized. Persons without teeth have less power of resistance to disease and many of them are often weakened for a long time. Even the best artificial teeth cannot perform the same function as natural ones, and in a great number of cases they function badly. Moreover, the extraction of the teeth is not a harmless operation. In addition to many complications arising from infected forceps, &c., I have seen cases in which bleeding lasted for many days with consequent anæmia, and the nervous system became much affected. In one case a female patient developed pneumonia soon after the removal of all her teeth. In some cases empyema of maxillary sinuses occurred. I know of cases in which death has followed the extraction of all the teeth. In one case a man, aged 20, died from tetanus as a consequence of extraction of several teeth.

Though the loss of teeth is a great misfortune, we may sacrifice them in order to save life or to get rid of some metastatic systemic disease. But have we any proved evidence that so many diseases are really caused by dental sepsis?

The very interesting bacteriological researches of Rosenow, Billings, Haden, Price, and some others, so far lack confirmation.

There is no pathological evidence for this theory. In cases of infected pulpless teeth or an alveolar abscess there is, as a rule, no communication with the general circulation. It becomes an enclosed infected area in the alveolus around the root tips with granulation tissue and granulated osteitis. By an extraction of such a tooth with an apical granuloma we usually find a small sac or mass with pus containing various bacteria. Therefore it is very doubtful whether any bacteria and toxins escape from such a local focus to other parts of the body. I have seen only the following complications which, in my opinion, might probably be related to dental sepsis: trigeminal neuralgia, empyema of the maxillary antrum, cervical adenitis, Ludwig's angina, and dental osteomyelitis. But I have never seen a case of disease of the circulatory or of the respiratory system, or of other visceral organs, or cases of septicæmia, septico-pyæmia, toxæmia, &c., due primarily to oral sepsis.

We know that patients, young and old, with pyorrhœa, or with alveolar abscesses, do not suffer from general and infectious diseases more than others with healthy teeth. It occurs in the experience of every medical practitioner that people recover from these diseases when oral sepsis is not even treated. In many cases with general infection, no local focus can be discovered. And in the case of occurrence of infection in a patient with dental sepsis there can usually be found another cause besides the teeth. The removal of all the teeth as well as of some other local foci, in cases which I have seen, has usually failed to relieve the patients, though some have recovered in spite of the extraction of the teeth. It has not preserved them from various infections; in regard to this, Rosenow, Billings and others allege that the occurrence of the disease after removal of primary foci is due to secondary foci.

The extraction of all the teeth or even of all suspected teeth, as a preliminary to treatment is also irrational, because, so far, it has been nearly impossible to prove that a certain metastatic disease is caused by oral sepsis. The blood examination and differential count of leucocytes or other laboratory methods do not prove the presence of a local focus.

Thus the theory of the relation of many diseases to oral sepsis is based, so far, only on clinical observations. There are on record hundreds of such cases. I will mention some of the cases recorded during recent years. In one of Haden's cases—a man with duodenal ulcer—there were three infected pulpless teeth. Two rabbits injected with cultures from one of them showed hæmorrhages in the gastric mucosa, some of which progressed to ulceration. In another case, that of a man suffering from periodical attacks of fever, hæmaturia and streptococci in urine, there was a pulpless tooth. In another case a woman with onychia had had attacks of iritis and pyelitis. All the pulpless teeth and the tonsils were removed. Bohan described a case of a woman with chronic ligneous thyroiditis. Three teeth, with abscesses, were extracted. In all these cases the conclusion with regard to the ætiological factor—infected teeth—is based only on experiments on rabbits. The same holds good with regard to the numerous cases recorded by Price in his book.

In the case reported by Hoxie of a man suffering from palpitation and symptoms of nervousness, the patient had carious teeth and hypertrophied tonsils. As the blood-sugar tolerance showed a great decrease, "it became evident that it is due to focal infection." In the cases recorded by Willcox, Troisier, Semon, Murray, Smith, Draper, and others, there is neither bacteriological, nor experimental, nor clinical evidence in support of their opinion that the particular diseases were really due to dental sepsis. The conclusion is only based on the old formula: *post hoc, ergo propter hoc* (see my paper). In many cases there was not even any indication of improvement after extraction of all the teeth.

CONCLUSIONS.

(1) There is no pathological, bacteriological, or even clinically proved evidence that dental sepsis is the cause of many diseases. Further investigations are necessary to prove this theory.

(2) The extraction of all the teeth is always contra-indicated and only does harm to the patient. It is an unnecessary experiment.

(3) In cases of gingivitis and alveolar pyorrhœa the gums and the teeth should be treated and only teeth beyond repair should be extracted.

(4) In some diseases of the head, above mentioned, oral sepsis may be suspected as the probable cause. Then a consultation with the dental surgeon and radiologist should be arranged and the focus dealt with.

REFERENCES.

- ASHCROFT, CUNNINGHAM, McMURRAY, and PEMBERTON, *Brit. Med. Journ.*, 1925, ii, p. 13. BILLINGS, "Focal Infection," 1916, New York and London. BOHAN, *Med. Clin. N. Amer.*, 1924, vii, p. 1069. DRAPER, *Amer. Journ. Med. Sci.*, 1925, clxix, p. 429. HADEN, *Med. Clin. N. Amer.*, 1924, vii, p. 1109. HOXIE, *ibid.*, 1924, vii, p. 1119. MURRAY, *Lancet*, 1926, i, p. 387. PRICE, "Dental Infection, Oral and Systemic," Cleveland, 1923. ROSENOW, (a) *Journ. Inf. Dis.*, 1915, xiv, p. 240; (b) *Journ. Amer. Med. Assoc.*, 1915, lxiv, p. 1969. ROSENOW and MEISSER, *Arch. Inter. Med.*, 1923, xxxi, p. 807. SEMON, *Pract.*, 1923, cxi, p. 199. SMITH, *Med. Journ. and Rec.*, 1925, cxxii, p. 207. STOLKIND, *Med. Press and Circ.*, 1921, cxi, p. 414. TROISIER, *Bull. et Mém. Soc. méd. Hôp. de Paris*, 1925, xli, p. 629. WILLCOX, *Brit. Med. Journ.*, 1923, i (repr.).

Dr. P. HAMILL

said that cases could be divided into two main groups: those in whom one had a proof—more or less satisfactory—that a focal infection was the cause of the patient's condition, and secondly, those in which one might regard it as a flank attack, diminishing the general health of the patient, and allowing some important condition from which he suffered to become unduly prominent. He saw a number of cardiovascular cases, and he thought it could be agreed that infected tonsils were an extremely important factor, probably in the causation, but at any rate in the maintenance, of cardiac disorders. All present must be familiar with the delicate type of boy, with a slightly dilated heart, who fainted on occasion, had a quickened pulse-rate, and frequent small rises in temperature. In many of these cases one could be reasonably certain that the circulatory system was sound, because on their good days these boys could join in the school games. Frequently one could find some septic focus, the removal of which produced dramatic improvement. It was commonly the tonsil which was the seat of the trouble. Similar factors might be at work in cases of grave myocardial disorder.

A medical man was invalidated from one of the Services; he had attacks of tachycardia. The speaker saw him in an attack once and electro-cardiographed him, and found he had a true paroxysmal auricular fibrillation, which had disappeared next morning. He had certain digestive disturbances, and it was felt that there was an infective focus in his alimentary canal, which was at least partly a cause of his condition. Careful examination, however, did not enable a diagnosis to be made. A year later he had a sudden attack of cholecystitis, for which he underwent operation, and since then his attacks had become fewer.

Another medical man, whose case the speaker watched closely, had attacks of what were regarded as paroxysms of auricular fibrillation, but as they occurred only at night electro-cardiographic confirmation was not available. The attacks ceased by the morning. He had also suffered from amœbic dysentery, and had attacks of colitis at intervals. Careful examination by X-rays showed dental root abscesses. The infected teeth were removed, and since then his health had become better; he gained weight, and in the last twelve months he had had only three attacks of auricular fibrillation, instead of, as formerly, one in every six or eight weeks.

Another man wore crowns and bridges in his mouth, and he (Dr. Hamill) saw him during attacks of paroxysmal tachycardia. He was not available for electro-cardiographs. Since his defective mouth fittings and bad teeth were removed, his attacks had diminished and, though over 70 years of age, he had since gained weight and was living an active life.

The connexion between infected tonsils and appendicitis was recognized.

Recently he had seen a case, again in a medical man, who had an indefinite intestinal

disorder—diarrhoea, uneasiness, &c. The state of his teeth seemed satisfactory, and his appendix was removed after much consideration. The appendix was not normal but not grossly diseased. He improved up to a point, and then had a pain in his jaw, sepsis was discovered in the antrum, which had previously been looked for but not discovered. That had been drained, and the patient was now very much better.

He agreed with those who objected to the ruthless extraction of teeth. Every tooth should be scrutinized, and only, if condemned, should it be extracted.

Focal sepsis was of great importance in cardiac conditions, when for instance a digestive upset caused much cardiac embarrassment. If foci of sepsis were eradicated the patient became a healthier individual and the organic disease embarrassed him less.

"Pain round the heart" and palpitation were quite common symptoms of sub-acute appendicitis, and in quite a number of patients sent up as heart cases, or coming of their own accord, gross disease of the appendix was found at operation.

With regard to organs which had an internal secretion, he understood Professor Murray to say he did not think there was any evidence that chronic sepsis affected the thyroid. But cases had been seen such as Professor Murray described in which infective processes exacerbated exophthalmic goitre. And it was not improbable that long-continued sepsis exhausted the thyroid and sympathetic side of the human economy. That was his own impression. Among the slides which Mr. Graves showed was one at least in which the obvious thyroid enlargement diminished when the source of sepsis had been cleared away. It was well known that an infected process embarrassed carbohydrate metabolism and diminished the efficacy of insulin.

Sir STCLAIR THOMSON (President)

said for the information of those who did not know how acute a focal sepsis could be, he would throw on the screen four charts which would speak for themselves.

The first was that from a case of acute pan-sinusitis. The gentleman was seized with an acute cold in the head, and he was in bed three weeks with suppuration in all the sinuses of his head. The only one of them which was treated surgically was the antrum, and that was washed out on the occasions shown on the chart. It was a streptococcal infection. The pain was so intense that the relatives believed he had meningitis. The case was seen by him (the speaker) in consultation with Dr. Farquhar Buzzard, who said there was only sinusitis. The sinuses ceased to suppurate, and a few days later he developed an abscess in his thyroid gland.

The following chart was that of a hospital nurse, who was warded under the speaker with acute left-sided multisinusitis. This yielded a pure culture of the influenza bacillus. No surgical treatment was employed in this case; the treatment was medicinal, together with rest and warmth, and she made a complete recovery.

The next chart related to another nurse, who was in the bed next to the patient just mentioned, and was warded at the same time. The diagnosis here, too, was that of influenza. Here there was a pneumococcus infection in pure culture. She had to be carefully watched for three months because, at the end of three weeks when the fever had passed off, there was still a little pus in the sinuses. She underwent no surgical or vaccine treatment. She got completely well.

The last case was interesting because it was that of a girl who had a slight sore throat. She was a healthy dairymaid, aged 17. She developed acute double sphenoidal sinusitis, and she died in consequence of developing thrombosis of the cavernous sinus. There were secondary abscesses in the neck. The sinuses were opened and drained, and from each of them streptococci were obtained. The actual cause of death was meningitis. Post-mortem examination showed pus in the anterior fossa and in the orbit. The picture exhibited showed the patient as she was a few days before her death, in the typical phase of complete external ophthalmoplegia, chemosis, &c. This showed how acute a sinus infection might be.

Professor G. R. MURRAY (in reply)

said there was not much for him to add, except to express his thanks to the other speakers in the discussion, from whom he had learned much, particularly as to the importance of focal sepsis in mental disease, a phase he had not very often encountered. He was very glad that, in addition to stressing the importance of dental sepsis, there had been uttered a healthy protest against the unnecessary extraction of teeth. He had himself seen many cases in which bad results occurred from unnecessary extractions. He agreed that the condition of each tooth should be separately judged, and that only those should be removed which were a source of focal sepsis.

Mr. HERBERT TILLEY (in reply)

took the opportunity of thanking the Council of the Society for having asked him to take a leading part in the discussion. He was particularly pleased to have been able to do so, because it so happened that the opener, Professor Murray, was his former house-physician when he (the speaker) was a clinical clerk in University College Hospital under Dr. Ringer. Dr. Murray had then taught him the elements of medicine and he had learnt from him again on this occasion.

The Royal Society of Medicine.

President—Sir STCLAIR THOMSON, M.D., F.R.C.S.

DISCUSSION ON HYPERPIESIS.

The Rt. Hon. LORD DAWSON OF PENN, G.C.V.O., K.C.B.

It would seem natural, at the outset of a discussion on the interesting subject of hyperpiesis, to make reference to Clifford Allbutt, a great master still inspiring our thought and stirring our affections. Knowing his objection to the word "hypertension," I will try to avoid it in my remarks, and will use instead the word "supertension," which he rightly preferred.

The choice of hyperpiesis rather than hyperpiesia as the subject of this discussion is, I suggest, a wise one; for the key to a disease and our hope of alleviating it lie in a study of its beginnings, and it is in accordance with clinical experience that the condition of supertension has no rigid limits, no defined boundaries, but passes gradually, often silently, into states of disease. Those states, when fully developed—the results, perhaps, of damaged arteries or defeated hearts—are better considered under their own headings, and may well be left out of our discussion to-day. In order to limit the range even further, I will omit direct reference to prognosis and treatment.

The first question I would propound is this: Is supertension necessarily associated with changes of structure? Is it, in its beginnings, a disturbance of function which may lead to changes of structure—or is it preceded and produced by changes of structure? One way to seek an answer to this question is to make inquiry amongst younger and apparently healthy people. In this way the perplexing association with arterio-sclerosis is avoided.

There is, I suggest, a group of people who have an over-responsive vasomotor nervous system, just as others are liable, for instance, to nervous dyspepsia and diarrhoea. It is part of their make-up, just as much as their external features. Such people are liable to transient supertension under physical or psychical stress. The rest pressure is commonly, though not always, above the normal, and this high reading is sometimes a family trait. Some seem to exhibit it under physical stress alone, though more often it is apprehension, anxiety to "arrive," ambition, which is the motivating cause. The link between the higher centres and the vasomotor centre is too intimate, and the latter responds to every "blast of vain doctrine."

Take, for instance, a medical examination of boys aged 14 to 15 at the beginning of their first term at school. I will select three boys, similar in their healthy appearance and cheerfulness and demeanour, whom I will call A, B and C. Two of them had a normal pressure. At rest, A's pressure was 125/60, and his pulse-rate was 78. After running up and down seventy-two stairs two at a time, his blood-pressure went up to 162/65, and his pulse to 114. After six minutes of recumbency, however, the pressure fell to 120/60 and the pulse to 100. Those figures are no higher than you would expect in a boy somewhat agitated on first going to school. The second boy was very similar. At rest: blood-pressure 110/65; pulse 85. After going up and down the seventy-two stairs: blood-pressure 135/70; pulse 104. After three minutes' lying down: blood-pressure 120/70; pulse 90. Most authorities will agree that the pressure of a healthy youth, after an effort such as I have described, should return to normal after about three minutes' rest. In many people older than these, a rest of three or four minutes suffices to bring back the pressure to their normal.

Now contrast these cases with that of the boy C, who was 14½ years old. To start with, his blood-pressure was 135/70. After seventy-two stairs it was 170/85, and his pulse-rate was 144. It was over twenty minutes before his pressure returned to its starting point. I must have taken six or eight observations, with every precaution to avoid fuss or trouble to him.

That boy, as I see him, is a potential hyperpietic. His vasomotor system is over-sensitive—too responsive. At present the supertension is probably transient, and the pressure is very likely capable of returning to the normal for his age; but he has within him, nevertheless, the makings of hyperpiesia. What is in store for him will depend on circumstances—how deeply ingrained this vasomotor responsiveness happens to be; whether his temperament is placid, or over-anxious and striving; whether in the hurry of life he becomes a slave to anticipation. It will be affected by his employment, whether strenuous and uncertain, or quiet and methodical: by his social life, whether cast in congenial or in discordant surroundings; by his physical habit, whether trim and restrained, or stodgy and relaxed; and by whether there is any tendency in his family to develop supertension. The balance of all those factors may be either for or against him as life proceeds. His tension may keep within the normal until the responsibilities of maturity and the metabolic imperfections of middle life come upon him. These, if they reinforce his tendencies, will make his pressure rise.

To make brief mention of some other examples of hyperpiesis in youth, I will refer to the examination of 580 undergraduates at Toronto. The average pressure amongst them was 126±71. Ten per cent. of them had a systolic pressure of over 140 and in this group the average age was 19. Alvarez¹ found in the examination of 1,500 undergraduates that over 20 per cent. had a systolic pressure of 140 or more. Amongst 650 children of ages from 10 to 17 examined by myself and colleagues fifty-two had a systolic pressure above 130. Some of those fifty-two were further investigated, and a few of them showed thickening arteries and signs of cardiac strain—a little displacement of the apex-beat, an enlargement of the heart evident to X-rays, accentuation of the aortic second sound and left-sided preponderance.

That is ample evidence, to my mind, that supertension—transient, intermittent or even permanent—does exist amongst the young. No doubt with many of them it is a passing phase, but not with all. Even some of the intermittent cases of hyperpiesis appear to produce cardiac enlargement with accentuation of the second sound, and left-sided preponderance. Are they (as I suggest) the result of over-responsiveness, a raised excitability of the vasomotor centre—a reaction to modern civilization and the pace of life? Strickland Goodall, who investigated 2,000 cases under the age of 40, found that the most frequent antecedent in the histories was scarlet fever. That would fit in with the infective origin of hyperpiesis, and be concordant with the contention that hyperplastic sclerosis of the intima is the chief change in hyperpiesia. But there are many cases of hyperpiesis without any history of scarlet fever; and is there not to-day, in the search for causes, rather too strong a bias in favour of infection? Do we give enough weight to the internal factor—the nature of the soil? Moreover, it is difficult to conceive that these groups of healthy young people, equal to any kind of work and play, are victims of an infective process.

I will next make brief allusion to over-responsiveness of the vasomotor centre in adults, and will avail myself of two cases from Frost's investigations. Both were the subjects of mental stress and anxiety. The first was aged 36. His rest pressure of 148 ultimately reached 220 under effort tests; whereas on a later day, when stress was absent, similar tests only raised it from 118 to 144, which is within the normal. This was a case of intermittent supertension—of excessive vaso-constrictor responsiveness.

The second case was aged 41. His rest pressure was 150/100; under effort test it was 246. This subject had moderate hypertrophy of the heart, so that structural

¹ Alvarez, *Arch. Intern. Med.*, September 1920, p. 381, July 1923, p. 17.

change had begun. In contrast to these, take a woman aged 35 with an anxious, worrying nature—a woman whose vasomotor centre has not this selective responsiveness, but who, by contrast, “feels abdominally.” Her rest pressure is 110/90, and easily falls to 100 under fatigue. After quick exercise it goes up to 155/90, returning after two minutes to its original level.

I suggest that the next stage in the development of hyperpiesis is that the rest pressure assumes a higher level. This is the form usually found in practice, either in the course of routine examination, or because the patient complains of headache, throbbing, or other symptoms. Such a raised rest pressure will vary in degree; in some cases it will be temporary and amenable to treatment, and in others it will be fixed and resistant to treatment. And here I would suggest that the diastolic pressure, which tells us the enduring strain on the arteries, is perhaps of greater importance than the systolic. If the diastolic is not above 100, and there is no advanced arterio-sclerosis, a systolic which is prone to rise easily need not disturb us unduly. One does not like a diastolic above 100 in an adult, and in youth one likes it round about 70 to 80.

The following example will illustrate fixed supertension in youth, and will transfer attention to the pathological view of the problem.

A girl, now aged 23, looks and feels well, and better than a year ago. She enters into work and play. Her sole disability is that she tires more easily than most; a full day's work is a little too much for her, and if she takes heavy exercise she is somewhat breathless. For safety, therefore, she has half-time employment; but she can dance and take part in the ordinary affairs of life. In early childhood she had scarlet fever. She has occasional headaches, but fewer than formerly. Her rest pressure is 250/150, and it has been at this level, to my knowledge, for several years. After running up and down seventy-five easy stairs the pressure rises to 280/150, returning to 240/140 in ten minutes.

Her rest pressure is fixed. I tried once to get it down: after a month in bed with careful dieting and drug treatment her rest pressure was lowered to 165. Then I got her about gradually, and, after a certain amount of training, I sent her out for a ten minutes' walk on the flat. At the end of that walk she had a pressure of 215. There it stopped, and the work of a month was ended in ten minutes. That is what happens to nearly all these fixed pressures, in my experience. Her younger sister has a rest pressure of 160/100, and both her parents have rest pressures on the high side. Her blood urea and functional renal tests are—in contrast to a case of interstitial nephritis—within the normal. There is an occasional trace of albumin in the urine and a few odd casts. Her radials are too palpable, but not hard: her heart is enlarged, the apex-beat being in the nipple line, and there is an accentuated aortic second sound preceded sometimes by a systolic bruit.

Now I will ask you to give attention to the minute anatomy of her kidneys. There are three things to be noted: thickening of the media of the interlobar and arcuate arteries (a pure hypertrophy); slight thickening of the intima of the smaller vessels; and patches of atrophic tubules. The outstanding feature is the thickening of the muscular coat, which is, I suggest, a reactive process, like enlargement of the heart, and follows on continued vaso-constriction. I suggest that the thickening of the intima of the smaller vessels is a slighter and later process. In the sections small vessels can be made out with the intima swollen and structureless, or again with splitting of the elastic layer and here and there focal areas of fatty degeneration. In short, there are the changes of hyperplastic sclerosis; but these are far less prominent than the medial changes. For the observations on the minute anatomy of these specimens I am greatly indebted to Professor Turnbull and Miss Russell, M.B., B.Sc., Beit Fellow at the Pathological Institute, London Hospital. For the inferences therefrom I am responsible.

On a future opportunity I shall publish the illustrations with Professor Turnbull's fuller report upon the structures these delineate. And I suggest that hyperplastic sclerosis is not a necessary feature—still less a cause—of the early stages of hyperpiesis, though at a later stage it plays an increasing part and may cause the tubal atrophy. This hyperplastic sclerosis may be the reason why the kidney seems sometimes to take charge in the later stages of this disease—I suppose we would call it hyperpiesia. And, curiously enough, this change is prone to select the vessels of the kidney, the pancreas and the spleen. In an analysis of seventy-two necropsies of patients dying of supertension, Fashberg found that the minute arterioles of the kidney were always affected, those of the spleen in 66 per cent. of cases, and of the pancreas in 50 per cent. Why the pancreas and spleen should be affected it is difficult to say. No pancreatic insufficiency has been noted. That the hyperplastic sclerosis develops in the course of hyperpiesis is shown by clinical experience, namely, that whereas hyperpiesis is apt to be followed by clinical arterio-sclerosis, the latter, in half the cases, is not associated with hyperpiesis. The two processes may hunt in couples, and when hyperpiesis has reached a certain stage. In middle life and later, when arterial degeneration is apt to occur, hyperplastic sclerosis may follow close behind, or may even coincide with the hyperpiesis. Therein lies the advantage of a study of youthful subjects.

To complete this line of thought, let me show you a contrast between the early case I have just shown you and a case at a later stage, for which I am indebted to my colleague, Dr. Parkinson. In the former (early) case the thickening of the media is the more marked feature, and the intimal change is relatively slight. At a later stage the thickening of the media is less apparent, and the intimal change is more apparent. Further, a study of the sections in the more advanced (Parkinson) case suggests a replacement of the muscular cells of the media by fibrous tissue, and it may be this is the process whereby the changes and thickness of the media become less prominent in the more advanced cases.

I have given this emphasis to hyperpiesis in youth in order to show that in its inception it is a functional disease—what I have called elsewhere “physiology gone mad”—and because in youth the problem can be kept clearer of athero-sclerosis. On the other hand the majority of cases make themselves apparent in middle and later life, though even here the proneness may have existed at a younger age. The association of hyperpiesis with the climacteric, with eclampsia, and with the blubber type of obesity, suggests some perversion or (as Clifford Allbutt said) some warp of metabolism. It is known that there are harmful chemical substances derived from protein in the upper intestine, but are not these more often depressor than pressor? It is said that pressor amino-bases are excreted in the urine. But has the presence of the guanidine base, for instance, reported by Major, been confirmed? The chemistry of this research, I have reason to know, is very difficult, and liable to error.¹ I think that all we can say is that we watch with interest the efforts of the biochemists to give us the key.

There is experimental evidence which suggests that too much importance has been attributed to both protein and salt intake. On the other hand, authorities like Pal and Newburgh think that protein food beyond the minimal amount is harmful. Is it not true clinically that moderation in eating and limitation to light food which is first cooked are of the most importance?

As regards the influence of such ætiological factors as meat, alcohol, tobacco and endocrine disturbance, Nador-Nakitit, investigating the details of 495 cases of hypertension, found ninety-three cases of renal sclerosis, 202 cases of various other diseases, and 200 healthy individuals. He could find no definite relationship between these factors (meat, alcohol, tobacco and endocrine disturbance) and hyperpiesis.

¹ A valuable investigation into the secretion of guanidine was undertaken by T. M. Seth, under Sir Frederick Gowland Hopkins, at Cambridge.

In conclusion: What are the beginnings, and what are the stages in the evolution of this condition? I suggest that the origins are several, although, once the process has started, the anatomical course is the same. Does hyperpiesis have its origin in functional change? Is it a result of exaggerated function, of over-excitability of the vaso-constrictor centre? If so, are hypertrophy of the media, and hypertrophy of the heart the earliest changes? Or, on the other hand, is this hyperpietic change due to previous infection? If so, is the next stage a thickening and degeneration of the intima? Or (as I suggest) is the earliest change hypertrophy of the media in early life? In middle life, is the first stage infection or perverted metabolism? And is the resultant hyperpiesis due to vaso-constriction or to intimal degeneration?

Those are important questions, not only from the point of view of knowledge, but also from the point of view of early and preventive treatment. If, for example, it is known early in life whether an individual has an excessive vaso-constrictor responsiveness, an exaggeration of a normal function, a great deal can be done to so guide and steer his life that the condition will never grow into a fully developed disease. My impression, on the whole, is that this condition starts in exaggerated function. (I do not say that the disturbance is in every case the same; in middle life it certainly is not.) Whatever the cause of that disturbed function may be, once it has become fixed and set, and is no longer transient and intermittent, I think that the subsequent anatomical changes which lead, by steady progression, to the developed disease, are probably one and the same.

PROFESSOR FRANCIS R. FRASER, M.D.

In attempting to present this subject of persistently raised arterial pressure, if we base the clinical features on physiological and pathological knowledge in the same way as we try to do for students, the difficulties of this presentation are numerous. In the attempt to manage cases by therapeutic measures, based on physiology and pathology, the difficulties are equally numerous. It may serve, however, to encourage the requisite observations, or to bring out observations already made, if we review briefly such physiological and pathological knowledge as offers clues to their elucidation.

The mean arterial pressure depends essentially on the output of the heart and on the peripheral resistance. Clinical observations, such as those reported by Lord Dawson, on school children, point to changes in the heart as being later in the sequence of events, so I propose to deal only with factors influencing the peripheral resistance.

In health the peripheral resistance is so regulated by elaborate nervous reflex mechanisms that an adequate supply of blood to all the tissues of the body is maintained. Of principal importance in these mechanisms is the vasomotor centre in the medulla. During healthy everyday life, brief variations in the mean pressure are continually occurring as the result of reaction to environment, and we have knowledge of certain actions and reactions that may be involved in these physiological adjustments. (1) An inadequate supply of blood to the vasomotor centre causes a rise of general arterial pressure through constriction of the arterioles of the body generally and of the splanchnic area in particular, so as to correct this inadequacy. (2) The vasomotor centre is stimulated also by afferent stimuli reaching it from the periphery, such as the stimuli giving rise to pain. (3) General arteriole constriction can be effected by the higher portions of the cerebrum also, since a rise in general arterial pressure is found in sudden emotional states, such as fear or anger, and in the state of anticipation of some event requiring sudden exertion. To what extent a sudden outpouring of the internal secretion of the adrenal bodies is responsible for this is still undecided, but it is certain that the injection of adrenalin into the circulation can produce this effect by acting on the peripheral neuro-muscular apparatus. (4) We must

conclude, therefore, that chemical substances, such as internal secretions in the circulation, can produce a rise in the general arterial pressure. From the anatomy and physiology of the circulation it is easy to see that (5) structural changes in the small arteries and the arterioles so as to constrict their lumen, such as those seen in diffuse hyperplastic sclerosis, will, if sufficiently widespread, raise the general arterial pressure, and that (6) structural changes in the blood increasing the resistance to flow, as in erythrocythæmia will have a similar effect.

On turning to the clinical aspects of persistently raised arterial pressure in the search for clues, cases associated with nephritis and with erythrocythæmia are well recognized, and in them the raised blood-pressure is considered, probably rightly, as but a symptom of the more fundamental and more important disease processes.

The relations of raised arterial pressure to degenerative changes in the arteries, and of renal disease to raised arterial pressure, are of great importance and interest, and the solution of these relationships will without doubt throw light on the whole problem.

It is natural that we should approach those cases in which the origin of the raised blood-pressure is not known, with the idea that in them also the raised pressure is but a symptom of more fundamental disturbances or disease processes. From the physiological and pathological considerations mentioned above the possible causes appear to fall under the following headings: (a) disturbances of the vasomotor centre itself; (b) influences at the centre from the higher portions of the brain or from the periphery; (c) circulating chemical bodies, including internal secretions, able to raise pressure by a peripheral action; and (d) unrecognized arterial or renal disease. It must be remembered, however, that persistently raised blood-pressure must have a persistent cause.

(a) It is unlikely that inadequate blood-supply to the vasomotor centre can be the cause in many cases without the origin of the inadequacy having been discovered in some, although it is conceivable that in a few of them abnormalities in the arteries supplying the centre could exist without being recognized. I know of no evidence in favour of this mechanism.

(b) How reflex stimulation of the centre from the periphery, or of the emotional or the anticipatory states, can result in a rise of pressure that is persistent it is difficult to see, but that there is such a connexion is suggested by the fact that long-continued mental and physical stresses have been recognized as frequently associated with this condition. The therapeutic success of rest cures, and of careful education in physical and mental hygiene, is also in favour of such a causal relationship. It is possible, through some adaptation similar to that involved in the establishment of "conditioned reflexes," that the frequently repeated exposure to physical and mental stresses that modern city life requires may result in a persistent vasomotor stimulation of psychic origin. If such an acquired mechanism is present in some of the cases, the explanation of the hereditary characteristics that are so frequently cited would be simplified, since Pavlov has shown that in successive generations the ease with which reflexes become adapted or "conditioned" becomes greater.

(c) The assumption of disturbances of internal secretion as a cause is supported by the number of cases that arise about the time of the menopause, and by those examples seen in adolescents in whom the condition disappears in adult life. The results of treatment suggest that infections and the hypothetical circulating chemical toxic substances may be at least contributory factors. The generally recognized association with over-eating, with over-indulgence in alcohol and tobacco, and the satisfactory therapeutic results of restricted dietary and reduced indulgence, suggest that in these cases also circulating chemical poisons are causes of the persistently raised pressure.

(d) It is probable that a number of cases of renal and of arterial disease are not recognizable in the early stages, and are erroneously considered as belonging to the

group in which no underlying disease is found for the raised arterial pressure.

It appears to me to be a mistake to conceive of a common cause for the group of cases that it has become the fashion to label by the term "hyperpiesia," even though the sequence of events, once the persistently raised pressure is established, is comparatively constant. I would suggest that the raised arterial pressure is the result of a number of factors, one or usually more than one of which are present in each case. Such investigations as those Lord Dawson has referred to, in which the cases in the early stages are sought for, can only be of great assistance in defining the causes of this condition. In every early case, before secondary changes have developed in the heart or arteries—if these really are secondary—careful note should be made of hereditary factors and constitutional make-up, of exposure to mental and physical stresses, of over-indulgence or of unbalanced dietary, of infections, and of evidence of disturbances in the internal secreting organs. In this way I believe we should obtain clearer views of the ætiology of raised arterial pressure and of the steps that must be taken to check or prevent it.

The recognition of the condition in the early stages can only be effected by the use of the sphygmomanometer, and I plead for the more extended practice of recording diastolic pressures. The mean pressure is what we really need to know, and it lies much nearer to the diastolic than to the systolic level. The systolic pressure is but a rhythmic increase of pressure, due to each heart beat, over the constant diastolic pressure, and is a measure of the systolic contraction of the ventricle. The diastolic pressure is a much better guide to the peripheral resistance.

DR. F. PARKES WEBER.

We hear a good deal about hyperpiesia being a direct or indirect outcome of the stress or wear-and-tear of modern civilized life. I do not believe that stress of life can be accepted as a cause of hyperpiesia in *normal* healthy individuals. Professor E. H. Starling¹ has admirably explained and experimentally illustrated that the normal brain needs a well-maintained blood-pressure and that, if there is danger of the blood-supply in the vasomotor centre and brain becoming insufficient, the blood-pressure of the whole body will be raised in order to maintain the blood-pressure in the brain at a sufficiently high level. When active participants in the serious business or strenuous pleasures of life reach a certain age, say, about 50 years, some of them begin to react to the stress of life by increasing blood-pressure. This, I take it, is in many cases because the cerebral circulation has become relatively defective owing to changes in the arterioles (and capillaries?) or because the nervous centres themselves have become blunted in some way (such as by chronic toxic conditions) and demand a higher blood-pressure to enable them to perform the (in some cases, ever-increasing) work demanded of them.

What are the individual types who about middle life react towards modern civilized life-stress by a gradually increasing blood-pressure, whilst others of the same age remain at the prime of their effectiveness and usefulness without any need of excessive blood-pressure? They are certainly not the constitutional neurasthenics and psychasthenics, whose nervous system in this respect acts as a safety-valve, shielding them from stress. Nor are they likely to be the chronic dyspeptics and visceroptotics, whose gastro-intestinal system is "shy of work," and reacts by pain or discomfort to any strain.

Those with middle-age high blood-pressure are in the majority of cases, I believe, rather fat than thin, and have habitually taken more food (with or without alcoholic additions and excessive tobacco-smoking) than their mode of life rendered advisable. In some cases, indeed, they may belong to families with familial tendency to high blood-pressure, and seldom or never to families (and I am sure that there are such families) with familial tendency to unusually low blood-pressure.

¹ Starling, *British Medical Journal*, 1925, ii, pp. 1163-1165.

Generally, as children, they have been "blessed" with a good appetite, and after puberty is over, when the body requires somewhat less food, they have not reduced their intake of food—perhaps they have even increased it, owing to improved financial means. There is a kind of vicious circle. Too much food leads not only to obesity, but, sooner or later, to a kind of toxic condition owing to inability of the digestive and metabolic systems to respond adequately to the excessive demands made on them. The kidneys and excretory system are overstrained and do their work inadequately. The result of all this may be that owing to a toxic condition of the brain or to inadequate circulation in the brain, or owing to more or less generalized disease of the arterioles (and capillaries?), especially in the kidneys, the general blood-pressure of the body becomes (probably increasingly) raised. Owing to subjective feelings of incompetence the diet is made more stimulating, and so the diseased condition progresses in a vicious circle, becoming more vicious until a grave breakdown of some kind occurs.

My above remarks refer merely to one aspect of the subject, but are, I believe, applicable to certain cases of a fairly ordinary kind. When hyperpiesia commences in *earlier* life the outlook is still graver, for in such cases the constitutional factor (whether it is familial or not) quite outweighs the exciting—and more controllable—factors. No wonder that the prognosis of habitually high blood-pressure is generally regarded as worse in young persons than in more elderly subjects! I would here note that in certain rare cases of excessively high blood-pressure in young subjects there is an "elderly type" of obesity present which one may term "precocious plethoric obesity," and which makes the patient look considerably older than the real age.¹

As to low blood-pressure in neurasthenics, thin visceroptotics and patients with pulmonary tuberculosis,² it is possible that the low blood-pressure may be partly cause and partly effect. Nevertheless, constitutional low blood-pressure (including familial cases), though perhaps predisposing to some diseases, tends apparently to some extent to ward off the dangers of stress, mental and otherwise, to which those are especially liable who have a constitutional tendency to high blood-pressure (whether familial or not). The weakly dyspeptic visceroptotics often out-live and ultimately out-work their more robust fellows. However, to try to produce an artificial low blood-pressure by the application of X-rays to the suprarenal capsules—or by the excision of the greater part of one of them—would seem unwarranted in early cases and likely to cause death if lowering of the blood-pressure were obtained in late cases of hyperpiesia. In families in which a definite familial tendency to high blood-pressure can be recognized, special care should, I believe, be taken in regard to the avoidance of excess of food, not only during middle life but much earlier, namely, at about the period of puberty and afterwards. This applies also to other precautionary methods for the avoidance of undue "stress." To prevent disease the patient must be "caught young."

I have had no experience of the treatment of high blood-pressure by the application of X-rays to the bone-marrow of the long bones, as suggested by S. W. Patterson,³ but it might well be tried in cases complicated by an excess of erythrocytes in the blood (the "hypertonia polycythæmica" of F. Geisböck). I do not think that a high erythrocyte-count in itself can be regarded as a sufficient explanation for high blood-pressure in any kind of case, the increase of blood-viscosity being doubtless compensated by dilatation of capillaries and arterioles.⁴

¹ Cf. F. Parkes Weber, "Cutaneous Striae, High Blood-pressure, Obesity, &c.," *Brit. Journ. Derm. and Syph.*, London, 1926, xxxviii, pp. 1-19.

² Pulmonary tuberculosis is generally associated with low blood-pressure, but not always. There are certainly exceptions to the rule, probably especially in patients who, owing to hæmoptysis in relatively early life, have long ago accustomed themselves to excess of food.

³ S. W. Patterson, *Lancet*, London, 1925, ii, pp. 1112-1114.

⁴ F. Parkes Weber, "The Blood-pressure in Splenomegalic Polycythæmia," *Brit. Med. Journ.*, 1925, i, p. 1108; G. E. Brown and H. Z. Giffin, *Amer. Journ. Med. Sci.*, Philadelphia, 1923, clxvi, pp. 489-502.

Dr. J. A. RYLE

referred to the remarkable pioneer contributions of Gull and Sutton, and Mahomed. It was clear from their observations that they appreciated that form of Bright's disease in which renal changes were of slight importance and the arterial changes of great importance. Mahomed was among the first to draw attention to the value of blood-pressure observations in disease; he regarded raised blood-pressure as an essential feature of the disease under discussion; and also emphasized the importance of looking for the beginnings of trouble in early life. Both Gull and Sutton, and Mahomed, referred to the cardiac hypertrophy and the occurrence of death from heart failure and cerebral hæmorrhage as opposed to uræmia.

Proceeding to discuss the question of diathesis in hyperpiesia he (the speaker) suggested as a definition of diathesis "a tendency, based on physiological and anatomical characters, to retain the impress of certain adverse stimuli." He had recently analysed a series of fifty cases of hyperpiesia in which he had obtained the history and made a careful routine overhaul himself. No cases were included of hyperpiesis due to renal disease or other than arterial disease. The systolic pressure was 170 or over in every case; the diastolic pressure 100 or over in every case but one. Forty-six per cent. of the cases were males, 54 per cent. females. The youngest of the males was aged 21, the oldest 68, the average age being 57.

Among the females the youngest was aged 28, the oldest 72, the average being 53. He classified the cases according to physical type. Sixty-two per cent. (both sexes together) were noted as "robust," healthy, stout, plethoric or "hypersthenic"; 18 per cent. as "average," 16 per cent. as "of poor physique," 4 per cent. as "lean and nervous." The anatomical features of the hypersthenic diathesis were a broad chest, a wide epigastric angle, frequently a healthy complexion and a short neck. The physiological characters were a hypertonic stomach and good tone of all plain and skeletal musculature. It had been shown in America that 10 per cent. of healthy students had a hypertonic stomach. He (the speaker) and Dr. Bennett had found a similar percentage of healthy students with hyperchlorhydria. Lord Dawson had quoted other figures suggesting that about 10 per cent. of healthy subjects showed a blood-pressure above normal limits for their age. He (Dr. Ryle) would therefore suggest that there was in certain individuals a physiological trend in the direction of hypertonus of plain muscle and so, incidentally, of raised pressure. These subjects often had great capacity for work and also were apt to over-eat and to grow stout on account of their lusty appetite. As a result they were more liable than others to acquire, and to retain as a permanency, a state of raised pressure.

In the group described as "of poor physique," and some of the "average" cases, infections appeared to play a much more important part. In the "lean and nervous" group emotional factors were common. Two small groups were, he thought, worthy of special consideration. One of these was the menopausal group, and seven out of the twenty-seven female subjects in his series were noted as menopausal cases. In these, probably, endocrine factors played a part. Finally there was the youthful group, but he regarded these as exceptional.

Of his three youthful cases one was a student, aged 21, with a blood-pressure of 180 systolic, 110 diastolic. He had various hyperpietic symptoms, including anxiety and a consciousness of his heart. At a later stage he came under the care of a colleague, he was suffering from obscure pyrexia and as it was thought that he might be tuberculous he was sent away for a long holiday. He had now returned to work, but the speaker had had no further opportunity of investigating his case.

The two remaining cases were females, one of whom he had watched for two years. She was aged 29, had a blood-pressure of 250 systolic, 150 diastolic. She was pale, unhealthy, easily tired, constipated, and had lived a life of consistent over-work since childhood. At times she had pyrexial attacks of uncertain causation. The other, aged 28, had a systolic pressure of 180, severe headaches, and, at one time, vomiting, for which an appendicectomy had been performed. Anxiety and mental unbalance were strongly-marked features.

He (the speaker) thought that these observations suggested that at present it was more profitable to study "the soil" in hyperpiesia than to seek for "the seed"—or in other words a specific causal agent—in the laboratory.

Dr. D. C. HARE.

THE VARIATIONS OF BLOOD-PRESSURE READINGS STUDIED UNDER
UNIFORM CONDITIONS.

I wish to call attention to the fact that the variations in blood-pressure readings in any individual under uniform conditions may be considerable, and that the range of these variations is greater than is commonly recognized to be the case. The point is important and must be taken into consideration when basing conclusions on isolated observations in individuals, and it also calls for caution in the acceptance of a lowered figure as being the result of any therapeutic measures which may have been adopted.

Variations obtained at One Sitting.

The figures I shall give are the variations in consecutive readings made at one sitting. These show that variations of both systolic and diastolic readings up to

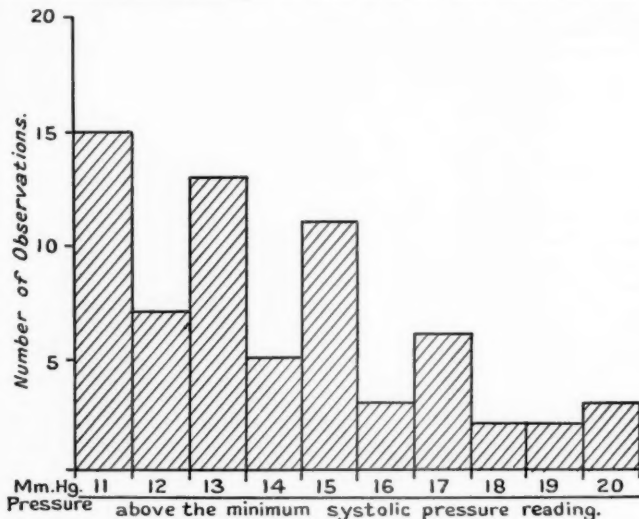


CHART I.—Incidence of variations of more than 10 mm. Hg pressure in systolic readings made at one sitting under uniform conditions in normal women. Total incidence 72 (31 per cent.); total sittings 228; total patients 60.

20 mm. may be obtained. In the tables I have only used figures of over 10 mm. variation. It would be generally acknowledged, I think, that variations of less than 10 mm. are of common occurrence, and that no importance can be attached to them, though not long ago I heard a speaker at a scientific meeting claim to have lowered the systolic pressure by 5 to 10 mm. as the result of treatment.

Source of Figures.

The figures are drawn from a series of normal women in whom I have been investigating cardio-vascular conditions during the course of pregnancy, and who are seen at intervals of about four weeks. All included in the series have been seen

at least three times, and many of them five or six times. The fact that the patients are pregnant is immaterial to the present point, as I am making no comparison between one period and the next, and am asking you to consider only the variations obtained at one sitting and within a few minutes of one another. The actual figures are on the low side of normal: Mean systolic 110-115; mean diastolic 70-75.

Conditions of Examination.

These are kept as uniform as possible. The patients are always seen in the morning, and rest, lying down, on a couch for at least twenty minutes before the reading is made. The pressure is read simultaneously in the two arms by two observers, the two arm bands being connected to the same mercury manometer. The first reading is always discarded and then three consecutive readings are made, giving six systolic and six diastolic readings in all. Patients become quite used to

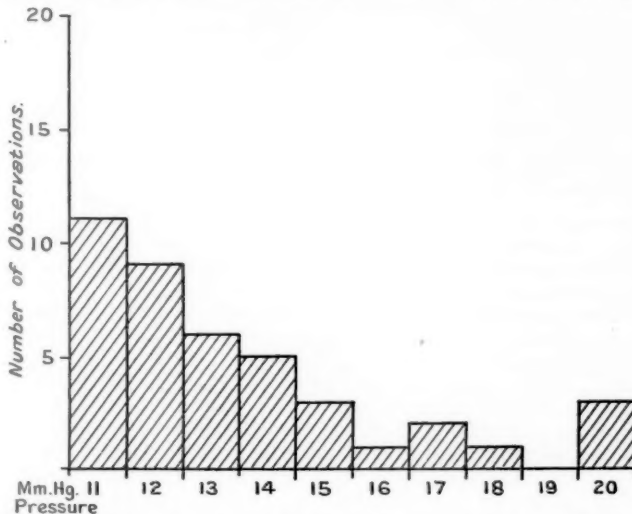


CHART II.—Difference in systolic blood-pressure readings obtained in *simultaneous* observations on the two arms. Difference greater than 10 mm. Hg pressure. Total incidence 42 (19 per cent.); total sittings 228; total patients 60. Right higher than left thirty-five times.

the process and the emotional factor can be excluded. The same observers, the same instrument and the same routine are used week after week.

Accuracy of Method.

I do not claim that the records obtained by this method are really accurate. I can only claim that a high degree of accuracy has been aimed at, and that they are results obtained under uniform conditions which should give more reliable results than it is usually possible to obtain in routine clinical work.

Diastolic Pressures.

Diastolic pressures are admittedly difficult of interpretation in some cases, and though uniformity of interpretation of the sounds is aimed at, this difficulty is certainly a factor in producing variations in the records. The figures of variations

are not very different from those for systolic pressures, though the range of variation is rather less.

Simultaneous Readings.

Simultaneous readings on the two arms may show a difference of 10 to 20 mm. pressure also. Right arm readings are higher than left in 83 per cent. of the records used for this table, so that this source of error can be greatly reduced by always using the right arm for making readings in routine clinical work.

Abnormal Pressures.

I have no figures relating to cases of abnormally high pressure. I do not know whether they would give a greater or less variation when studied in the same way. It is a point worth investigation.

Publication of Details of Method.

In publishing accounts of blood-pressure investigations too little attention is paid to the conditions of the examination and the methods used. It would increase the value of the results if reference were always made to these points.

Conclusion.

In conclusion I would re-state my point that blood-pressure readings obtained by ordinary clinical methods of auscultation vary with some frequency up to 15 mm. Hg, and that this variation must be considered together with the other better recognized factors, such as emotion or exertion, causing physiological variations.

Sir JOHN BROADBENT

said that it might be taken for granted that some families showed a tendency to high blood-pressure and some to low. There was no high blood-pressure apart from some degree of peripheral resistance. It was unreasonable to assume that high blood-pressure was necessarily due to the nitrogenous excitants that accompanied kidney trouble, for this was often absent. There must be some common cause. High blood-pressure might be responsible for kidney trouble. Even if the vasomotor centre were over-excitabile there must be some toxin to excite it; adrenalin and thyroid extract would cause hyperpiesis, but there was no evidence of hypertrophy of either thyroid or suprarenals in the majority of cases. High blood-pressure and renal disease had many symptoms in common, but death from coma and convulsions was very rare in the former. It was impossible to state what was the toxic substance, but to discover the cause of hyperpiesis we should look less to the kidney and more to deficient metabolism on the part of the liver. The French had given the name "uræmic moiety" to an unknown nitrogenous constituent which was found in excess in the blood in uræmia; this moiety might have some bearing on hyperpiesis.

Dr. HENRY ELLIS

said that it must be recollected that in the two types of condition insisted upon there was a different chemical composition. In the first there was always a relatively high phosphoric acid in the urine, in the second there was always a deficiency of that substance in the urine. In the major group, the sthenic, there was always in the urine an equality between the ratio of the free acid and the ammonia-combined acid. In the second group there was a 3 to 1 ratio between the ammonia-combined acid and the free acid. In the latter group in the cases he investigated he was certain there was a toxic element. In the balanced group of equal ratio one was apparently dealing with an acid intoxication; there was an excess of acid in the organism, and if hydrochloric or other acid were given to the patients the blood-pressure would frequently rise very rapidly. In one case the blood-pressure was

140, and six doses of hydrochloric acid given in three days sent the pressure up to 250. If a case had a 3 to 1 ratio between the ammonia-combined acid and the free acid in the urine, one could be almost certain that it was toxic. He believed the condition of intestinal toxæmia to be the most common form. The rise of blood-pressure in the other group seemed to be accounted for by a difficulty of elimination of acid in the urine. That was why the blood-pressure, once having risen, could not easily be brought down. The diastolic pressure was practically the statement of what the intercellular condition really was: it represented the pressure that was needed to keep the intercellular condition normal in the fluid surrounding the cell. By suddenly altering it, one brought the fluids into a condition wanting in equilibrium; hence it was dangerous to try to lower the diastolic pressure. High blood-pressure hyperpiesia was very probably a viscosity question. A nerve cause would be temporary, but a blood cause, which meant a difficulty of elimination, would be permanent. Insurance society experts would say that the death-rate of the high pressure cases was high. Until the urine was systematically examined for the ammonia-combined and free-acid ratio, he did not think the means would be at hand for differentiating the other two groups.

Dr. J. CRIGHTON BRAMWELL (Manchester)

said that Professor Fraser had emphasized the importance of the diastolic pressure, and in that matter he (the speaker) strongly agreed with him. A heightened diastolic pressure not only raised the mean pressure—the important factor to be considered, from the point of view of the nutrition of the tissues—but as the diastolic pressure increased it rendered the arterial wall very much less extensible, and so entailed an even greater rise in the systolic pressure in order that the heart might maintain its output. The output of the heart given by a diastolic pressure of 80 and a systolic of 120 might suffice for ordinary moderate exercise; but if the diastolic pressure rose to 120 or 130, the systolic pressure must be put up to something like 240 or 250 in order to maintain anything like an equivalent cardiac output. So that a rise in diastolic pressure not only placed a great additional strain on the heart and endangered any diseased arteries, so increasing the risk of cerebral hæmorrhage, but it also acted in another way by limiting the oxygen supply to the tissues. When an artery was stretched by a high diastolic pressure, it became so inextensible that even an enormous increase in the pulse pressure would only maintain a sufficient cardiac output to meet the requirements of very mild exertion. And if to that was added a doubling or even trebling of the resting heart rate, the heart still was unable to meet the demands of the active muscles during severe physical exercise.

There was one rather interesting compensatory modification of the cardiac mechanism which sometimes came into play in these cases; it was well illustrated by the case to which Lord Dawson had referred that afternoon, and which he (Lord Dawson) had kindly given the speaker the opportunity of studying. In order to enable the aorta to accept the ventricular output, the duration of the ejection phase of systole was prolonged, or at least that part of this phase during which the pressure was rising in the aorta. In that way some of the blood which was discharged into the aorta had time to escape to the periphery before the heart attempted to discharge the remainder of its contents. But for that, the output of the heart would be much diminished. In those cases the anacrotic form of the sphygmogram was of considerable prognostic importance. If the ventricle was capable of prolonging systole and so allowing part of the blood to escape to the periphery before it discharged the remainder of its contents, the heart muscle must be in a fairly satisfactory condition. But if the heart muscle was failing, the sphygmogram more closely resembled the ordinary form, in which the highest pressure in the aorta was reached at an early stage, six- or eight-hundredths of a second after the commencement of systole. In the

latter the prognosis was not so favourable as in those cases giving a sphygmogram of a more anacrotic type.

Dr. HALLS DALLY.

I propose to deal with one aspect only of hyperpiesis, namely, that of classification, since at the present time there are considerable grounds for regarding this as essential.

In the consideration of any problem a loose or inexact terminology constitutes a real and definite hindrance to progress. Much lack of unanimity results from the same term being used by various writers in different senses, and from the use of a multiplicity of terms to convey a single idea.

In the course of investigations upon arterial pressure during the past fifteen years, on comparing and contrasting the views of numerous authors, one obvious fact emerges, that seldom is the same name employed in two consecutive papers to mean the same thing. High arterial pressure, "hypertension," hyperpiesis, and even hyperpiesia, are often indiscriminately and inextricably confused with arterio-sclerosis or the effects of kidney disease, myocardial changes and infective processes.

For the moment I am concerned solely with definitions and not with interpretations. By "hyperpiesis" I mean a rise of arterial pressure from any cause whatever, whether temporary or permanent, physiological or pathological.

Already the classification of hyperpiesis has been attempted from several aspects, none of them entirely satisfactory. An aetiological classification can be only partial, since we are not yet cognizant of all the primary causes. An anatomical classification does not take us far, whilst a pathological one deals solely with the end-results of vital phenomena, which are all-important for further detailed investigation. Physiology renders us valuable aid, but since the problem of hyperpiesis rests upon a physical foundation, sooner or later we are bound to return to physics as the basis of the proposition.

In physics there are only two sources of rise of pressure—*increased force or increased load*—and from the physical standpoint we may regard the circulation as composed of a central pump system, comprising the heart and great arteries, an intermediate reservoir, and a peripheral outflow system, comprising the series of pipes through which the circulating fluid is distributed throughout the body. Pressure is varied by the force of the pump, the size of the distributing vessels and the character of the circulating fluid. (1) If the force of the pump is increased, and the diameter of the pipes remains the same, the pressure is augmented; conversely, if the force of the pump is decreased, the diameter of the pipes remaining the same, the pressure is diminished. (2) If the force of the pump remains the same, and the character of the circulating fluid is unchanged, then, if the diameter of the pipes is reduced so as to lessen the outflow the pressure is again raised, and if the diameter of the outflow pipes is increased, the pressure falls. Such peripheral resistance in physical parlance is termed the load. Hence, if the nature of the fluid remains the same, a rise of pressure must be caused either by an increase of the central pump force, or by an increase in the peripheral resistance.

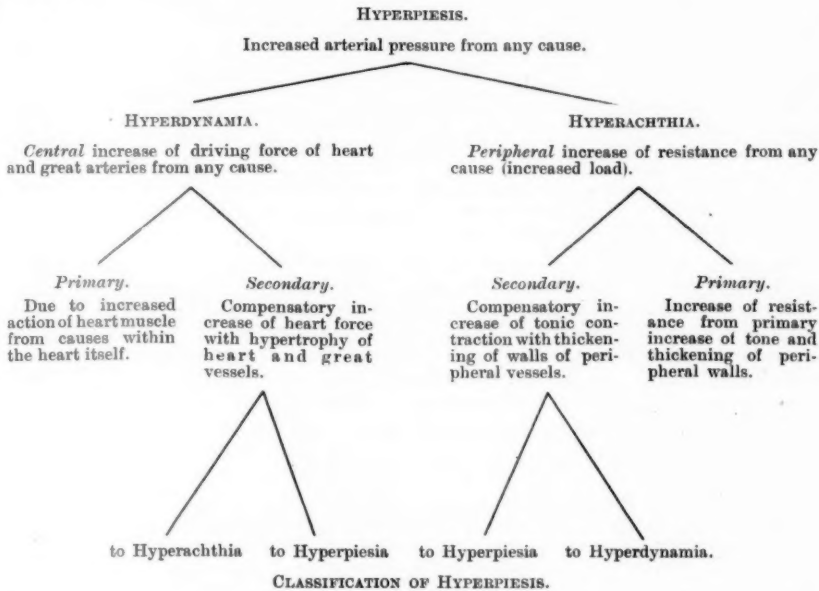
The central system may be affected in one of two ways: primarily, by direct increase of the pump force; or secondarily, by an increase in peripheral resistance, which calls for increased action on the part of the pump, so that the increased peripheral resistance may be overcome by an augmented central pressure.

The peripheral system may also be affected in one of two ways: primarily, when there is a direct diminution in calibre of the peripheral vessels, or a change in their resiliency in the direction of increased rigidity; and secondarily, where such

alterations take place in order to compensate augmented dynamic action of the central pump which necessitates contraction or rigidity of the peripheral vessels.

Hence, reduced to the simplest formula, the primary causes of increased arterial pressure are two in number: (1) a central dynamic cause, due to increased power of heart and great vessels; (2) a peripheral load increase through contraction or thickening of the vessel walls, any secondary cause being only compensatory to the primary one.

We are now in a position to translate these physical terms into equivalent terminology, and the expression of these conditions will be found in the accompanying table of classification:—



Starting with hyperpiesis, as including all forms of high arterial pressure from whatever source arising, this main heading embraces three subsidiary divisions, two of which, hyperdynamia (central) and hyperachthia (peripheral), are of known causation, and a third, hyperpiesia, whose origin is still *sub judice*.

Primary hyperdynamia results from any cause which necessitates augmentation of the driving force of the heart and great arteries, and in time leads to hypertrophy.

Secondary hyperdynamia results from a hyperachthia, which causes the heart and great vessels to hypertrophy, for example, a damaged kidney produces a secondary hyperdynamia in the rest of the circulation. Similarly, arterio-sclerosis causes a secondary increase in the force of the pump, because of the greater difficulty met with in driving the blood through sclerosed arteries.

Primary hyperachthia results from any cause which increases peripheral resistance, and is associated with hypertonia, i.e., an active contraction of the smooth muscle of the vessel walls, which, in turn, if long continued, induces vascular hyperplasia.

Secondary hyperachthia occurs in response to a primary or a secondary hyperdynamia, as in the case of a primary arterio-sclerosis.

Thus secondary hyperdynamia and hyperachthia will naturally result from hyperpiesia, acting either centrally (hyperdynamia) or peripherally (hyperachthia). In true hyperpiesia the heart hypertrophies to meet the pressure, and the vessels of the periphery become thickened for a similar reason in a combined process of degeneration and repair. In this way the circle is completed, as shown in the table, which includes all possible variations of hyperpiesis, and can readily be adapted to low pressure states by the substitution of "hypo" for "hyper."

The chief difficulties encountered in the literature of hyperpiesis to-day arise through lack of definition of the terms employed, or through these terms being subjected to individual limitations or extensions of signification. To this welter of confusion the French and American schools have added by their constant usage of the word "hypertension," which, unfortunately, has only too frequently been adopted also by our own writers. I was glad to hear Lord Dawson's reference to this in his opening remarks, for against the use of this hybrid I wish also to record a vigorous protest. In any event "supertension" would be more correct, but, as the late Sir Clifford Allbutt remarked:—

"Tension is the stress which tends to split the artery longitudinally or transversely, and such stress is at more advantage when the vessel is relaxed . . . the 'blood' cannot be tense in any but an abstruse mathematical sense."

Hence, from the ætiological point of view, as well as the philological, I submit that it would be wiser to abandon the term "hypertension" altogether.

The above classification represents an attempt to attach to each term a definite meaning, concerning which there can be no misconception. In order to avoid the use of long and cumbersome phrases, I have ventured to introduce the two new words, hyperdynamia (*ὑπέρ, δυνάμις* = over-action) and hyperachthia (*ὑπέρ, ἄχθος* = over-load). Hyperpiesia is maintained in Allbutt's original signification, being confined to rises of pressure of unknown origin.

DR. G. W. GOODHART

said he desired a little information, from the standpoint of morbid anatomy, concerning the two slides which Lord Dawson exhibited. As far as he remembered, Dr. Geoffrey Evans emphasized the fact that the morbid change in hyperpiesis was a thickening of the intima. The slide from Lord Dawson's first case was from a biopsy, and it showed great thickening of the media. In connexion with the second slide, Lord Dawson said the intimal thickening might be a later stage of the same process. That seemed rather difficult to believe; but assuming it to be so, if the change were a progressive one, there ought to be found, in the second case, a certain number of vessels showing Lord Dawson's medial thickening. He asked whether there were also, in other vessels of the patient, some changes in the media such as Lord Dawson showed in the first slide.

DR. KINGSTON BARTON

said that Lord Dawson had done well in having devoted his opening address chiefly to the blood-pressures found in young people, as in this way a knowledge of normal pressures was brought into a proper relation with those that were abnormal. He (Dr. Barton) had always considered that all cases of very severe high blood-pressure were simply the expression of unmitigated changes in the kidneys, invariably associated with chronic fibrosis accompanied by every variety of cirrhosis. For it was possible for there to be enormous fibrosis and yet there might be very little cirrhosis. But the higher the blood-pressure the more assuredly would there be cirrhosis and its accompanying hypertrophy of the heart, with the intense changes in all the arteries

of the body. It should not be forgotten that it was possible for very great changes in blood-pressure to occur and yet for the condition to be only physiological. But let that high pressure once become a really persistent feature, and there must then be present an organic condition to account for it. All hospital records for many years showed that post-mortem examinations of people between forty-five and fifty-five years revealed 50 per cent. of actual kidney affections, although many other causes were given on the death certificates. And of these cases in which there were recognized changes in the kidneys, generally only 25 per cent. were diagnosed during life. Below and above those ages there were fewer cases of actual renal disease. With regard to treatment, there were only two methods that might reduce excessive high pressure. (1) Lying in bed; and it required a good deal of treatment to bring about any lasting benefit. (2) Calomel was the only drug that had any effect. No doubt in former days doctors kept their high-pressure patients alive by the weekly dose of blue pills and black draught. But in these long-standing cases of high blood-pressure, if the physician tried seriously to reduce the pressure he generally only ended the life of the patient. For this high blood-pressure was simply a violent effort of nature to keep the patient alive, as this was his only means of tackling the problem of getting rid of his nitrogenous waste products. In all cases of pure cirrhosis there was never any albumin present, because there never had been any parenchymatous nephritis, and it was on this evidence of no albumin that up to recent times it was held there was no renal disease. No case of hyperpiesis had been properly inquired into unless the heart had been examined under the X-ray to see what amount of hypertrophy was present, and until the blood-urea had been estimated and the urea concentration tests applied. It was even possible for there to be normal specific gravity and quantity of urine, and even a normal quantity of urea, and yet in all these cases the time eventually came when the polyuria and the hypertrophied heart were established, both of which indicated interstitial changes in the kidneys. In spite of over-eating, over-worry and other probable and real causes of all this very high blood-pressure, it seemed to him (Dr. Barton) that renal changes would always be found if looked for. In re-reading the works of George Johnson, Burdon Sanderson, Gull and Sutton, W. Howship Dickinson, and Mahomed, of Guy's, one could not help realizing that we had made no advances in the past fifty years. Even Gull and Sutton held the field in microscopic work bearing on blood-pressure. But if Dr. Mahomed had only lived a few years longer he would probably have cleared up all these debateable points. His work on the pre-albuminuric state of Bright's disease showed that he fully recognized hyperpiesis. It was a great pity that the use of the sphygmograph, as inculcated by him, had so completely fallen into disuse.

Lord DAWSON OF PENN (in reply)

said it always seemed to him that the difficulty of altering accepted terminology was very great; there was always the tendency to lapse back to terms to which one had grown accustomed. Hence all such changes must of necessity be slow and be in the nature of a compromise. In the last book Clifford Allbutt wrote it was clear he was aiming at what he termed a compromise.

With regard to what might be called the fully-developed disease, when a patient was seen at that stage, with a fixed high pressure, and with a growing disability of some kind, he supposed all would agree that there were structural changes underlying the clinical symptoms, and yet that even when this stage had been reached the kidney was more or less in command. Then there supervened, he considered, the condition of hyperplastic sclerosis of the kidney, and the patches of tubular atrophy and replacement fibrosis of which he had spoken, and which had been so well delineated by Dr. Geoffrey Evans. The diminishing amount of functioning kidney substance still further increased the already existing cardiac hypertrophy, because

the kidney, like the brain, was then in the capacity of a master-organ, which meant that it would bring to itself blood at any cost. There followed, to use Clifford Allbutt's excellent term, the state of "defeated heart and defeated brain." So that there was a gradual cardiac insufficiency arising from pure hypertrophy. If, on the other hand, the arteries became degenerate and there was a sudden rise of pressure, hemiplegia might occur. If such patients caught an intercurrent infection, they did not long survive. But they stood operations rather well. It was the low-pressure patient about whom he was anxious when that patient was operated upon. There were various roads along which the established disease could be approached. His theme had been that derangement of function was often a necessary precursor to the established condition, but not always—for there was no such thing as "always" in medicine. In over-responsive cases it was not necessary to assume the operation of a toxin; this state of affairs was a potential one for the production of hyperpiesia. He did not suggest that all the school children of whom he spoke would become hyperpiesics; in fact, he was convinced that many did not. Among the 650 London school children there were a number about 17 years old, the age at which a sense of responsibility usually arrived; these were working keenly for an entrance to the Oxford Higher Examination; if they passed this, they would obtain a good chance of entering the University. Hence in those cases there was operative an incentive from within as well as from without. Among these pupils the incidence of high pressure was about two and a half times that of the average. Some of these adolescents had since either passed or not passed, but they had, after the examination, resumed something like a condition of stability and had lost their high pressures. When these young people entered the competitive arena of life, it was possible that their high pressure would return, but probably not in all cases. He was willing to admit that infection might yield a similar result, but the numbers were too great for infection to have played any prominent part. The cases at a later stage should be viewed from the condition of the intima and the media of the vessels; the degeneration and thickening of the intima was a dominating feature of the picture, the hypertrophy of the media being of less importance. In the case of the patient of whom he had particularly spoken, and who was still alive, he believed that in ten years' time a condition would be found more nearly approaching that described in Geoffrey Evans's paper, i.e., that the change in the intima would have increased. Why did he (the speaker) find the media so thick in his case? Why was not the media thick in the more advanced cases? The suggestion was that the thickened media of the present would be gradually replaced by fibrous tissue later on.

He was interested in Dr. Ryle's remarks about hypersthenic cases. Dr. Ryle seemed to think that the condition could originate in a functional change. At one time he thought the hypersthenic cases constituted the larger group, but he had slowly abandoned that idea.

Dr. Parkes Weber seemed inclined to doubt whether psychical causes could exercise anything more than a slight influence in the production of high pressure in middle life; this scepticism however was unsupported by much available clinical evidence. Anxiety had been well defined as "fear spread out thin," and it could be seen in the type of man who hustled, used up every minute, and even when travelling seemed unable to relax. Such a man was striving to crowd too much into life. The fact was that the tissues could not alter quickly enough to respond to the quickened pace of life.

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JOINT DISCUSSION No. 1.

Sections of Comparative Medicine, Obstetrics and
Gynæcology, and Tropical Diseases and Parasitology.

DISCUSSION ON INFECTIVE ABORTION IN CATTLE AND
ITS RELATION TO MALTA FEVER.

Professor JOHN EYRE, M.D.

DURING the past decade a number of observations and experiments relating to *Bacillus abortus* on the one hand and the organism which is regarded as the causative factor in the production of undulant or Mediterranean fever on the other, appear to indicate that the relationship existing between these bacteria is extremely close and suggests a new interpretation of results obtained by earlier workers. The trend of present-day opinion, especially so far as relates to our transatlantic cousins, is to regard the two organisms, if not absolutely identical, at any rate so closely related as to demand for them a new genus, *Brucella*, in that very cumbersome and illogical classification they have recently evolved.

It is my duty this evening briefly to relate the main points in connexion with the two diseases that form the subject of our discussion, in such a way as to emphasize the agreed resemblances and to accentuate what are, at any rate in my opinion, the main differences.

Of the first I have no personal knowledge and my conception of the clinical picture is based upon the writings of veterinary surgeons, chiefly those of Buxton (1923) and Wilson (1913).

CONTAGIOUS ABORTION.

Symptoms.—Infective, contagious or epizootic abortion of cows is a highly infectious disease which rapidly spreads through whole herds, affecting especially the younger animals. The infection presents a very indefinite clinical picture so far as concerns the period between the moment of infection and the catastrophic termination of the pregnancy. There are no definite premonitory symptoms save that, if the cow is in milk, the secretion is usually diminished, and may be so altered as to resemble colostrum, but there may be the usual signs of approaching labour; the vulvar labia are swollen, the mucous membrane congested, and there is much glairy mucus which may be tinged with blood. Immediately before and during parturition a peculiar, opaque, yellowish, flocculent, vaginal discharge makes its appearance. There is a thick, glairy, yellowish or chocolate-coloured, odourless exudate which collects between the uterus and the chorion; there is a gelatinous œdema of the foetal membranes, and the foetal cotyledons appear as though macerated, opaque, and of a dull greyish colour. The embryo, now functioning as a foreign body, is expelled—a termination which usually occurs between the third and the seventh month. This act is followed by a thin, yellowish, or thick, greyish, purulent discharge and the common sequel is a catarrhal or purulent condition of the uterine mucosa, which maintains the discharge, in the absence of treatment, for a considerable time. The health of the cow is not apparently impaired and the mortality of the disease is *nil*; but the animal either remains sterile, or repeatedly aborts soon after service—generally within two months. Antibodies, such as agglutinins and complement-fixing bodies, can be demonstrated in the blood and in the milk.

Microscopical examination of the discharge shows numerous small bacilli, often apparently unassociated with any other organisms, either free or heaped together in

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dense clumps, many of the latter being collected within distended cells. Some of the bacilli are as long as tubercle bacilli; others, particularly when clumped, are 1μ or less in length and resemble cocci.

The path of entry of the infective virus is most usually that of food, infected with amniotic fluid or after-birth, representing a distinctly large dose of virus. The bedding may also carry infection, becoming contaminated with the vaginal discharges from infected cows, amniotic fluid, or foetal membranes. The males apparently act as carriers, and infection of the cow with *Bacillus abortus* may take place during service by males who have previously covered infected animals or who are themselves infected and excrete the bacilli in their seminal fluid.

Tissue Localization.—The causal organism can be isolated from the spleen, liver, testes, and the seminal vesicles of the infected bull; and from the spleen, liver, and the uterine discharges, as well as from the milk, of the cow. So far I have not found any record of observations on the urine. The membranes, cotyledons, amniotic fluid, and stomach contents of the infected foetus as a rule give pure cultures.

The incubation period is obviously not accurately known, but so far as one can gather from the literature, which places it from 33 to 230 days (and it appears to be customary to include the whole of the period intervening between service and the abortion), the average time is about 126 days. A point of interest in this connexion is that the earlier the infection takes place during pregnancy the longer the abortion is delayed; if infection occurs late in pregnancy then the animal may abort within a few weeks.

MEDITERRANEAN FEVER IN THE GOAT.

Turning now to undulant or Mediterranean fever as it occurs in the goat, there is similarly at first no very sharply-drawn clinical picture—at any rate for many years. My opportunities for study have been limited to the infection as it occurs naturally in the Maltese Islands, where the herds are already in part heavily infected and presumably, in part, naturally immunized; and to the experimental production of the disease in healthy normal goats selected from the uninfected members of flocks, or recently-dropped normal kids.

The infected animal appears to be healthy, is well-nourished, shows no tendency to abort and yields a plentiful supply of milk—a supply by no means curtailed even when the said milk is simply teeming with the infective organism. Nor, so far as one can make out, is there any marked contraction of the period of lactation. It is these very facts that render it so difficult to convince the Maltese goatherd that his animals can be suffering from any disease; but—and this, to my mind, is an important point—when once a milch goat is naturally infected, the infection continues from year to year until the death of the animal; the infection apparently becomes quiescent *during* successive pregnancies, but the excretion of the infective organism in the milk bursts out with renewed vigour with each successive lactation. Incidentally, the same description would apply equally to *melitensis* infection of the cow—as it occurs in Malta. In the advanced stages of the disease the animal is obviously out of condition; it wastes, lactation fails, and frequently it is affected with a hard, brassy cough that reminds one of the aneurysmal cough in the human subject.

In addition to the symptoms mentioned above, the infective organism occurs from time to time in the blood and is excreted in the milk and urine. Specific agglutinins and complement-fixing bodies are present in both the blood and the milk.

The path of entry is usually by cutaneous inoculation, either from contact of abraded surfaces with infected urine in the pens or with infective milk through the hands of the milkman. Infection by feeding has been successful experimentally, and there is no reason why the ingestion of infected fodder should not be a natural mode

of transmission. Finally, I have expressed the opinion elsewhere that infection also occurs during the service of healthy dams by infected sires.

Tissue Localization.—The causal organism can be isolated from the blood, spleen, liver and gall-bladder, kidney, urine, inguinal and mesenteric glands of infected goats, and from the udder and milk of the infected milch goat. It cannot be detected in the tissues of the kid newly born of an infected dam—indeed, such a kid appears distinctly resistant to infection for many weeks after birth.

The duration of the *incubation period*, based upon a mass of experimental details, appears to vary from seven to thirty days.

UNDULANT FEVER IN MAN.

When we turn to the clinical picture of undulant fever as it occurs in man, here we have a definite disease which, although rarely fatal (mortality 2 to 3 per cent.), gives rise to illness of a protracted type.

Symptoms.—Apart from the ambulatory cases, which exceptionally yield a history of a few days' "fever," but usually present no evidence of infection save the presence of the causal organism in the urine and specific agglutinins in the blood, the disease may be defined as a septicæmia, endemic in tropical and subtropical areas, running an acute, subacute or chronic course of indefinite duration, lasting for months or even years, and characterized by lack of constant symptoms other than slight or severe pyrexia—continuous, intermittent or remittent—with marked tendency to repeated relapses or "waves" of pyrexia, during which the symptoms originally present may recur with undiminished severity, accompanied or followed by emaciation and neuritis, and by certain metastases, such as synovitis, parotitis and orchitis.

Path of Entry.—In the majority of instances the ingestion of infective food, usually goat's milk or milk products, is the determining cause of the infection. In goatherds infection commonly occurs as the result of cutaneous inoculation. I have elsewhere adduced experimental evidence pointing to the possibility of infection during sexual congress.

Tissue Localization.—The organism can be demonstrated in all the tissues of the body in septicæmic cases, and in all types; it has on occasion been isolated from the spleen pulp, the blood, the urine and faeces, and the milk.

The incubation period varies from five to sixteen days.

In contrasting these three clinical pictures it is obvious that the mode of infection is practically identical in all three types of case. The protracted character of the infection is another point of similarity; but the outstanding feature of *Bacillus abortus* infection in the cow is the certainty with which the abortion results. So far as my own observations in an endemic area have gone I find that this does not happen in the goat infected with *Micrococcus melitensis*, but it is stated by some observers (Mohler and Eichhorn, 1911; Dubois, Della Vina, 1914) that when an infected goat is introduced into a healthy flock in a virgin district the disease rapidly becomes epidemic and subsequently endemic. In the early days of this endemicity abortion is to be noted as a frequent and often the only sign of the presence of the disease; moreover, Evans, 1923, produced abortion in forty-five days in a cow by injecting it intravenously with *Micrococcus melitensis*. In the case of the human subject, Hughes, writing in 1891, remarks, "Attacks of this fever (i.e., undulant) have not caused abortion in pregnant women in the few instances which have occurred in the practice of the writer"; and in my Milroy Lectures (1908) I, too, stated that "pregnancy frequently synchronizes with an attack of Malta fever and the patient remains unaffected, although lactation is frequently curtailed."

As both Hughes and myself observed the disease chiefly in Malta, it may be suggested that we were not sufficiently in contact with the native population to be familiar with what occurred in the infected women, and that the number of European

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women open to observation was too limited to warrant any sound opinion. But to this I would reply that both of us were in close touch with Maltese obstetricians and with Maltese hospitals, and were therefore in a position to obtain information relating to cases, if any occurred, in which abortion took place. With regard to Europeans, in 1905, Shaw, who analysed the cases that occurred in the Services, including Service women and children, for the years 1898 to 1904, showed that 30 per cent. males were infected, with a mortality of 3·3 per cent.; and 71·6 per cent. of the women became infected, with a mortality of 6·8 per cent. In other words, relatively more women than men were attacked and also acquired the infection in a more severe form. The average number of women (who, being the wives of the rank and file of the Army and Navy, were for the most part of the child-bearing age) was 498 for each of the years with which he was dealing. Yet, a couple of years later, when I was making inquiries in all directions with the object of setting out the individual symptoms observed in a large mass of material on a percentage basis, no mention of abortion was made by any of my confrères.

COMPARISON OF THE SPECIFIC MICRO-ORGANISMS OF THE TWO DISEASES.

BACILLUS ABORTUS.

Morphology.—A short, slender, pleomorphic rod with rounded ends; individual cells may be so short as to appear coccoid. The diameter is about $0\cdot5\ \mu$, the length varies from $0\cdot5\ \mu$ to $2\ \mu$ or $3\ \mu$. It is non-motile. It does not form spores.

Staining.—It is readily stained with the ordinary dyes, but it is Gram-negative.

Cultural Characteristics.—The first growth of a strain from pathological material in artificial media presents difficulties; it is, however, often favoured by incubation upon horse-serum agar under reduced oxygen tension, or in an atmosphere containing 10 per cent. CO_2 , but when accustomed to artificial culture aerobic growth is abundant on all the ordinary media. An agar-slope culture of a readily-growing strain shows an opalescent growth after twenty-four hours' incubation, which becomes heavier during the next day or two. It is a lustrous, moist growth with a sharply defined margin. Crystals begin to form in the agar after five to six days' incubation. On agar plates after two days' incubation colonies like tiny dew-drops appear on the surface of the agar. They gradually become opaque as they continue to increase in size during ten or twelve days' incubation, when, finally, the largest colonies attain a diameter of about 6 mm. In the depths of the agar there are two kinds of colonies—small, bluish-white, circular colonies, about $\frac{1}{3}$ mm. in diameter, and opaque, lemon-shaped colonies, about $\frac{1}{3}$ mm. long. In agar-shake cultures there is an abundant surface growth, but no growth beneath the surface. The agar just beneath the surface growth is rendered white and opaque. In broth cultures a faint clouding is visible after twenty-four hours' incubation. During the next day or two the clouding becomes heavier, but the broth never becomes heavily clouded. There is no surface ring or pellicle. After several days a sediment begins to precipitate. In litmus milk the only change is a slight alkalinity apparent after several days' incubation; this reaction never becomes pronounced. On potato there appears a slight glistening growth of a brownish colour. After several days' incubation the potato itself takes on a brownish tinge.

Biochemical Reactions.—(1) Gelatine is not liquefied. (2) None of the commonly used fermentable test substances are attacked. (3) Both urea and asparagin are decomposed with the production of ammonia, but the reaction in asparagin medium is often slight. (4) In broth cultures there is a reduction of the hydrogen-ion concentration equal to about 0·7 or 0·8 pH. This reaction is fairly definite and characteristic. The initial hydrogen-ion concentration of the broth may vary over quite a wide range in either direction from the neutral point without affecting the result. In nitrate broth there may be a slight reduction of nitrates to nitrites. (5) Indol is not produced in tryptophan media.

MICROCOCOCCUS MELITENSIS.

Morphology.—*Micrococcus melitensis* is an extremely small spherical coccus, not exceeding $0.4\ \mu$ in diameter, or a slightly ovoid cell, measuring $0.4\ \mu$ by $0.5\ \mu$. In old broth cultivations chains of ten to fourteen individuals may be found. It is non-motile, but exhibits very active Brownian movement. It does not form spores.

Staining.—It is readily stained by the ordinary dyes, but is Gram-negative.

Cultural Characteristics.—*Micrococcus melitensis* is readily isolated from pathological material by means of solid or liquid media, but it is a slow-growing organism. An agar-slope culture of a readily-growing strain at first consists of discrete colonies; these rapidly coalesce to form a moist, shining growth, which is at first white or pale yellow, but which with age turns amber and finally a distinct brown. On agar plates, after twenty-four hours' growth, the organism produces a ground-glass appearance on the surface; at forty-eight to seventy-two hours discrete colonies, resembling minute drops of water, are visible. The size of the colonies is inversely proportional to the number present on a plate; when moderately numerous a colony will attain a diameter of $1.5\ \text{mm.}$ at the end of a week, the maximum diameter (but rarely attained) is $5\ \text{mm.}$ In the depths of the agar, colonies are biconvex, with entire edges and finely granular surface. Colonies, when young, are translucent; at four days they become opaque white with a slight opalescence by reflected light, and pale yellow to pale amber by transmitted light. With age the colour passes from rich amber to light brown or even to dirty slate brown. In broth cultures very faint clouding is noted after twenty-four hours' incubation; during the next day or two the broth becomes denser and the upper layers of the fluid in a tube are denser than those below. At seven days a white deposit has begun to form. There is no surface ring or pellicle. In litmus milk the only change is definite alkalinity, which becomes quite pronounced by the end of four or five days. On potato the growth appears as a moist film, white to pale yellow in colour at the end of five days. Microscopically, the cocci are larger than those grown on agar, and are associated with numerous involution forms.

Biochemical Reactions.—(1) Gelatine is not liquefied. (2) Dextrose and lactose exhibit a faint alkaline reaction at the end of a week. (3) Other usual fermentable substances are not attacked. (4) In nitrate broth there is no reduction of nitrates to nitrites. (5) Indol is not produced in tryptophan media.

To contrast the responsible organism in each of these infections: *Bacillus abortus*, which was isolated by Bang in 1897, was described from the first as a bacillus, short it is true, but occasionally showing forms so short as to be coccoid in nature. In discharges from the cow it appears as a bacillus.

The *Micrococcus melitensis*, isolated by Bruce in 1887, was originally described as a coccus, and it appears as a coccus, in pus, milk and urine from infected individuals or animals. The exceedingly minute size of that coccus has always been insisted upon—the diameter being given as $0.3\ \mu$ to $0.4\ \mu$ by the bulk of observers who have isolated their strains from human cases of undulant fever. It is true that in old cultures and in very slowly-growing cultures (such as those on gelatine) forms were noted in which the length was often twice or even three times that of the diameter. These appearances I have always regarded either as the natural elongation of the coccus prior to division, or, alternatively, as involution forms.

To digress for a moment—that the appearance of elongated forms amongst other cocci is often sufficiently striking to impress the bacteriologist will be appreciated when I remind you that somewhere about 1900 Andrewes was describing the bacillary form of the *Streptococcus longus* and warning his students against confounding it with the *Bacillus diphtheriæ*. Also, some years later, Goadby, from his study of the *Streptococcus viridans*, actually proposed the name "*Streptobacillus mallæ*" for this organism.

American workers, however, regard the bacillary forms as representing the real shape of the organism and the coccoid forms, presumably, as involution forms; the drawings and photographs that they reproduce certainly give this impression. But from their descriptions and their photographs I, personally, fail to recognize the organism with which I am so familiar. The early subcultures of one of the strains I now have in my laboratory are almost spherical in shape, and their minute size is still retained; and until convincing proof is obtainable, I still adhere to the designation "micrococcus."

Again, the examination of these organisms by dark-ground illumination leaves no doubt in my mind that the *Micrococcus melitensis* is a coccus and the *Bacillus abortus* a bacillus; for in the vigorous Brownian movement which has always been a feature of hanging-drop preparations of the *Micrococcus melitensis* the excursions of individual cocci can best be described as zig-zag, to-and-fro movements within a limited space. With the *Bacillus abortus*, however, we have a totally different picture; there is a refractile granule towards the pole of each individual bacillus, resembling that seen in the pneumobacillus of Friedländer under similar circumstances, and the Brownian movement is that which is typical of a non-motile bacillus; it comprises a head-over-heels, somersault movement, like the acrobat's hand spring, and is limited to one spot.

I propose to make no detailed comments on the cultural reactions of the organisms. For my part, I should not consider the appearance of the cultivations of the *Bacillus abortus* upon solid media as suggesting more than a passing thought as to their identity with similar cultivations of the *Micrococcus melitensis*. In its earlier stages *Micrococcus melitensis* is white, and only with advancing age does the peculiar amber colour which is so typical of these cultures make its appearance; *Bacillus abortus* gives a yellowish film from the first, and the colour deepens rapidly to a light brown, with no glistening amber stage.

The next question that arises is, how did these two organisms come to be regarded as so essentially similar? The supposition arose from the correlation of a number of isolated observations.

Thus Schroeder and Cotton, in 1911, drew attention to the presence of *Bacillus abortus* in 14 per cent. of the cow's milk samples they inoculated into guinea-pigs, and showed that the organism was excreted by the animal even when there was no obvious lesion of the udder. McFadyean and Theobald Smith, in 1912, also found that guinea-pigs inoculated with raw cow's milk developed certain lesions which were due to infection with *Bacillus abortus*. These observations were confirmed by Zwick and Krage in 1913, and Fleischner and Meyer in 1917.

Larsen and Sedgwick (1913), and Ramsay (1915), found that the serum of 17 per cent. and 6 per cent. children's sera reacted positively to *Bacillus abortus*.

Kennedy in 1914, and also Bassett-Smith, showed that the milk of some London cows possessed the power of agglutinating laboratory cultures of *Micrococcus melitensis*.

The knowledge of these facts led to inquiries being made by Nicol and Pratt (1915), and Coolidge (1916), into the possibility of the infection of man by *Bacillus abortus*, when they showed that the blood-serum of some individuals possessed the property of agglutinating *Bacillus abortus* in fairly high dilutions. Eventually, however, they came to the opinion that there was no definite proof of this.

Nicoll, Burnet and Conseil also emphatically denied this possibility on the complete absence of effects when they injected seven men and two monkeys intravenously with large doses of living *Bacillus abortus* cultures. So also did Williams and Colmer in 1917, who investigated the complement-fixation reactions in the abortions of women, with special reference to the *Bacillus abortus*, with completely negative results.

According to Skarić (1922), contagious abortion is rife in some parts of Austria, yet there is no undulant fever to be observed in man in those same areas.

But as the result of much careful work in Rhodesia, Bevan (1920) suggested that undulant fever in that district is caused by *Bacillus abortus*, and in this he is followed by Duncan and Fleming (1924).

The presence in the blood of man of agglutinins for *Bacillus abortus* and in the milk of cows for *Micrococcus melitensis* prompted Miss Evans (1918) to undertake a serological investigation of these two organisms. At the outset she attempted rather too much, since she included in her inquiry the *Bacillus bronchisepticus*—an organism of the coli-typhoid group associated with distemper in dogs; and in this connexion it is interesting to note that Orpen regards *Bacillus abortus* and *Micrococcus melitensis* as allied to the *Bacillus faecalis alkaligenes*. Apart from this, however, Miss Evans clearly showed that *Bacillus abortus* antiserum, when tested against six strains of *Bacillus abortus*, caused partial agglutination in a dilution of 1 in 1,280 with four, with complete agglutination in lower dilutions. The other two strains of *Bacillus abortus* were partially agglutinated in the 1 in 2,560 dilution. Four of six strains of *Micrococcus melitensis* were partially agglutinated in the 1 in 1,280 dilution. Therefore, *Bacillus abortus* and *Micrococcus melitensis* were agglutinated by the *Bacillus abortus* antiserum in practically the same dilutions.

Later, the question was taken up by a number of different workers, and it now seems clear that immune "abortus" serum will agglutinate not only *Bacillus abortus*, but also *Micrococcus melitensis*, and, conversely, that immune *melitensis* serum will also agglutinate *Bacillus abortus*—in each case the actual antigen being agglutinated in slightly higher dilutions by its own serum; whilst absorption experiments show that the antigen is able to remove all the agglutinin from its own serum, but not quite all of the agglutinin from the "cross" serum—in other words, a sufficiency of the specific agglutinin remains behind to cause the agglutination of the related organism in low dilutions. Feusier and Meyer (1920) fully confirmed these results, as have many others since.

These observations therefore indicate the existence of a similarity in protoplasmic structure of these two organisms even closer than exists between many members of, for example, the well-defined "coli-typhoid" group, and their importance cannot well be disregarded.

To complicate matters, however, Burra (1919), working in Malta, showed that the serum from six cases of Mediterranean fever, which agglutinated *Micrococcus melitensis* in dilutions up to 1 in 1,600, also agglutinated *Vibrio cholerae* in dilutions up to 1 in 200; and the serum from three goats infected with *Micrococcus melitensis* did exactly the same thing.

Again, cases have been recorded from time to time of double infections of undulant and enteric fevers. In some instances both organisms have been isolated from the patient in question, but in several the diagnosis of typhoid has rested upon agglutination reactions. When the serum from such cases shows a high titre for *Bacillus typhosus* the diagnosis is probably correct, but it is no uncommon thing, in my own experience here in England, to find cases of streptococcal septicæmia which give a positive agglutination reaction with the typhoid bacillus in dilutions as high as 1 in 200—even when there is no clinical evidence of typhoid fever and no history of a previous prophylactic injection of antityphoid vaccine. All of these facts suggest that in the present state of our knowledge it is unwise to place implicit reliance upon agglutination and absorption tests.

To turn to another aspect of the significance of these observations, it will be recollected that every now and again a case in man has been described as a *melitensis* septicæmia, where the individual had not been in the habit of consuming goat's milk (such a case as that described by Duncan, 1920), or had not resided in or

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even passed through a region where the disease occurs; and the possibility is suggested that these are really cases of infection with *Bacillus abortus* derived from cow's milk.

Now it seems quite clear that the consumer of cow's milk might ingest a sufficiency of the *Bacillus abortus* to give rise to a pyrexia resembling Malta fever, and I think I am right in saying that in none of these sporadic cases of so-called Malta fever has the *Micrococcus melitensis* been isolated from the blood-stream. The diagnosis has invariably rested upon the presence in the patient's blood of agglutinins assumed to be specific for *Micrococcus melitensis*. On the other hand, these agglutinins may merely be the evidence of a passive immunity derived from the ingestion of *Bacillus abortus* antibodies present in the milk of infected animals.

I trust that I have said enough to show that there are many inconsistencies and discrepancies urgently demanding "experimental" attention, and that many links must be added to the chain of evidence before those of us who are familiar with undulant fever and its causative organism as it affects man can give our whole-hearted support to the thesis that *Bacillus abortus* and *Micrococcus melitensis* are identical organisms.

INFECTIVE ABORTION OF CATTLE IN RHODESIA AND ITS POSSIBLE RELATION TO HUMAN HEALTH.

[Communicated by Mr. L. E. W. BEVAN (Rhodesia)].

In November, 1921, I read a paper on this subject before the Southern Rhodesia Veterinary Association.¹ I pointed out that the disease known as infectious abortion of cattle existed in Southern Rhodesia, and was caused by the *Bacillus abortus* of Bang, and that serological tests indicated that it was identical with the specific abortion of cattle in other parts of the world.

I also drew attention to the fact that certain cases presenting symptoms resembling undulant fever had occurred in Southern Rhodesia in human subjects who, as far as was known, could not have obtained infection from goats, but had resided on farms where cattle were suffering or had suffered from infectious abortion. I found that the serum of such patients would agglutinate *Bacillus abortus*, and that the serum of cattle would agglutinate *Micrococcus melitensis*. But I had to admit that, while circumstantial evidence pointed to the infection of man by the *Bacillus abortus* of Bang, and scientific tests up to a point supported the suspicion, the final proof was not available.

Notwithstanding the publicity given to this communication a similar association between infectious abortion of animals and undulant fever of man has only once since been recorded elsewhere, namely by Keefer, in Baltimore, Maryland, U.S.A. This was a case of Malta fever occurring in a patient who had not been out of the State of Maryland, had not drunk goat's milk and had not been in contact with goats. He had, however, drunk much cow's milk and had eaten large quantities of cheese. It is significant that the patient was a technical worker in a laboratory, but it is stated that he did not come into contact with cultures. The type of organism isolated was *Brucella melitensis*, variety *abortus* (Evans). Evans showed that the strain from the Baltimore patient was serologically identical with strains from bovine sources.

The practical experience of veterinarians generally does not, however, support the view that the bovine infection is transmissible to man. At the recent Pan-African Veterinary Conference the matter was seriously discussed. Dr. P. R. Viljoen, who represented the Department of Veterinary Education and Research for the Union of South Africa, said:—

I do not know any reason for considering these two diseases to be identical in any way. In Great Britain where they have such extensive outbreaks of abortion in cattle whose milk

¹ *Trans. Roy. Soc. Trop. Med. and Hyg.*, 1921-22, xv, pp. 215-231.

is used by European people all over the country, Malta fever is practically unknown. In this country also, milk from cows infected with contagious abortion is used very extensively and yet one never hears of any ill-effects ensuing.

Nevertheless, the fact remains that cases of undulant fever continue to occur in Southern Rhodesia in men, women and children, who cannot have become infected from goats, but who reside, or have resided on farms or areas where cattle are or have been infected with the organism causing infectious abortion. In a table kindly supplied by the medical department is a list of cases admitted to hospitals in Southern Rhodesia during the past four years, and, on analysis, fifteen out of thirty-five patients are known by the writer to have come from areas where infectious abortion of cattle exists, or has existed, or to have consumed dairy products from infected herds.

Therefore it must be admitted that there is increasing evidence that in Rhodesia the undulant fever of man is in some mysterious manner associated with infectious abortion of cattle, and I submit that if this is so in one country it may be so in another. If, in any circumstances whatever, this insidious disease of cattle which is prevalent throughout the world, can become infective to man, it is a matter of the greatest importance, and one which should receive the most careful consideration of our professions.

It may be well, therefore, to discuss the matter more fully with a view to ascertaining the reason why the bovine disease in this country should have become infective to man. Let us first consider the cause of the disease in cattle in this country. In 1914 I proved that the serum of infected animals would agglutinate strains of the *Bacillus abortus* of Bang which I had obtained from the Royal Veterinary College, London, and from the Veterinary Laboratories of British East Africa and the Union of South Africa. This was an observation of considerable interest, since it showed the wide distribution of the *Bacillus abortus* and the remarkable uniformity in its agglutinating properties. Later (in 1921) I demonstrated that the serum of man suffering from undulant fever contracted in Southern Rhodesia would similarly agglutinate these various strains.

But although the organism infecting cattle is *Bacillus abortus*, it may be that we are dealing with a strain of that organism having peculiarities not revealed by the agglutination test. This introduces the question as to how the disease originated in this country. It is held by some that it has existed for generations in our indigenous cattle, which in course of time have become more or less resistant to it, but that, with the introduction of new blood in animals imported to improve the native stock, the disease has become exalted in virulence. If this were so, it is doubtful whether the herds which have been bred up from a foundation of native stock would have reached their present numbers. But I have recently received for experimental purposes fourteen native cows obtained from a district in which they have not come into contact with imported stock, and the blood of two of them has given a marked agglutination reaction. Unless this is due to some circumstance of which I am not aware, it certainly points to what I propose to call a "native strain" of infection. Natives have also stated that abortion was known to occur among their cattle before the advent of the white man: but such statements are unreliable. They may relate to sporadic cases—which under the methods of herding and breeding practised by the natives are numerous—and not to any specific disease.

It is certain, however, that infection has from time to time been imported from outside, notably in cattle from Northern Rhodesia, from Cape Colony, and also from Great Britain. We have therefore various strains of *Bacillus abortus* to deal with. But no matter from what district of Rhodesia the serum of infected cattle is obtained, it will agglutinate all the strains of *Bacillus abortus* which I have been able to obtain from other laboratories.

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With regard to the organism met with in man, Dr. L. J. Orpen, Bacteriologist to the Public Health Laboratory, Salisbury, has carried out some very interesting tests to determine its identity. In his annual report for the year 1923, he states:—

... the strains of organism obtained ... were compared with strains derived from European cases of Malta Fever, and from both European and Rhodesian contagious abortion. They were all exactly alike in shape, staining and cultures. ... A number of rabbits were then inoculated for a month, their serum prepared and absorption tests made, with the following results: It was found that all these organisms are of the same genus (which is now called *Alkaligenes*, e.g., *melitensis*, *A. abortus*, &c.), but that while European Malta fever is due to *A. melitensis*, the strains from both Rhodesian Malta fever and from contagious abortion were identical, i.e., the cases of Rhodesian Malta fever examined were due to infection with the organism of contagious abortion of cattle.

It would therefore appear that if there is any peculiarity of the organism which renders it pathogenic to man, it cannot be demonstrated by serological methods.

Burnet, in Algeria, has carried out investigations with many strains of the *Micrococcus melitensis* and *Bacillus abortus*, and has come to the conclusion that the two are one species. In his experiments *Bacillus abortus* proved more virulent for guinea-pigs, but less so for monkeys, which could resist doses one thousand times greater than those required of *Micrococcus melitensis* to infect them. Later he found that various strains of *Bacillus abortus* from foetal calves and pigs were non-pathogenic to man, and also that *Bacillus abortus* was not pathogenic to macacus monkeys.

The whole subject is very obscure, but it would appear that these organisms belong to one large group, with *Bacillus abortus* at one end and *Micrococcus melitensis* at the other, and that the pathogenicity of the various members of the group depends upon unknown factors the methods of passage and transmission of which are probably of great importance.

If, as I have previously suggested, there is a "native strain" of infection in this country, it is easy to conceive that such might have originated from a strain of *Micrococcus melitensis* which in the course of years—under the conditions which obtain in the native kraal, where goats, sheep and cattle are always in close contact with man—might have become adapted to cattle, and that man and cattle in due course might have become tolerant to it. To carry the idea further, such a strain might have become exalted in virulence by passage through imported cattle and their progeny, and again become pathogenic to the human subject, more especially to the European who would not possess the immunity acquired by the native of the country.

In 1921, when the disease in man first attracted attention, the majority of cases occurred in the Marandellas district and in districts to which cattle from Marandellas had been taken. Since then the majority of cases have come from Salisbury and its vicinity. In these areas the strains of infection are probably of "native" and South African origin. But no cases have been admitted to Enkeldoorn, Gwanda, Sinoia and Fort Victoria hospitals, although infectious abortion of cattle exists in those districts.

It is interesting to note that even on farms where the disease of cattle is severe, cases of human infection are never numerous. It rarely happens that more than one member of the family is affected. Sometimes it is a man, sometimes a woman, and rarely a child. In at least two instances the residents on an infected farm have escaped, while a visitor, or a recently arrived farm-pupil, has become infected. In the table previously referred to, out of a total of thirty-five cases, twenty-six are those of men, five those of women and four those of children. Among the male cases occur those of a postmaster, a teacher, a doctor, a mine manager, an engineer, a store-keeper, three civil servants, one engaged in the timber trade, two butchers and twelve farmers.

It is generally believed that the disease is contracted from infected milk or dairy produce, but if so it is difficult to understand why on some farms the man has become infected and not the women and children. If, on the other hand, infection is contracted by contact with cattle, or through the dust of the cattle-sheds or kraals, it is strange that in some instances the women have become infected and not the men. To explain these extraordinary circumstances it has been suggested that as the result of frequent exposure to mild infection, immunity is set up and that it is those who do not possess this immunity, or those whose resistance is broken down by some other cause, who contract the disease. The victims, however, are not always the weakest; in some instances they have been the most robust members of the family. The disease is not so prevalent throughout the country that the population generally can have become immune. If it were so, visitors to the country would run a grave risk. As far as is known none of them have become infected.

It is suggested by Orpen that "... in man infection by feeding with milk might fail, while inoculation of the blood-stream by a biting insect (which has been in contact with infected milk or dung) might succeed." This idea is attractive in that it offers a possible explanation for the exceptional features of the disease in this country. It may be that the solution of the problem rests with the entomologists. Bassett-Smith has pointed out that "... the conditions that are present in parts of America are in many ways analogous to those found in South Africa." It may be that the insect life is similar.

The clinical features of the disease in cattle in Southern Rhodesia are similar to those met with in connexion with infectious bovine abortion in other parts of the world, except that, occurring as it does, chiefly among range cattle, abortions are not so frequently met with as in countries in which cattle are more closely confined. Indeed, it frequently happens that the presence of the disease is only suspected by an exceptionally low "calf-crop," an unusual number of cases of retained placenta, a growing number of barren cows, or of cows returning to the bull. In dairy cattle, or those under closer observation, the manifestations of the disease are as elsewhere.

I am informed by the members of the medical profession in Salisbury that the disease in man does not differ from Malta fever, except that the temperature does not always conform with text-book descriptions. Not infrequently cases are at first mistaken for malaria or typhoid until blood examination and agglutination tests reveal the true nature of the disease. The chief symptoms appear to be pyrexia, headaches, anæmia, swollen spleen and liver, and pains in the joints. Neuritis and sciatica, and occasionally orchitis, follow. In one case recently returned from treatment in England, the vesiculæ seminales are apparently involved. This is of some interest, since Schroeder has shown that in bulls chronically infected with *Bacillus abortus*, lesions are found in these bodies. It is a remarkable fact that patients improve when they leave Rhodesia and live for a time at sea-level. This has become the favourite form of treatment and is undoubtedly the most successful.

Lastly, with regard to the measures adopted by the medical and veterinary authorities in dealing with this very difficult situation; when the specific character of the disease in cattle was realized, steps were immediately taken to cope with it. Cattle owners in Rhodesia have learnt wisdom in a bitter school: twice since the occupation of the country their stock has been decimated, first by rinderpest and then by East Coast fever. They would submit to almost any restriction rather than risk another disaster. They therefore readily complied with the requirements of the Veterinary Department, which made infectious abortion a notifiable disease. When the disease is proved by the agglutination test, the application of which is rendered easy by the "pipette method" (described by me in the *Journal of*

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Comparative Pathology and Therapeutics, xxviii, No. 4, December, 1915), the herd is placed in quarantine until six months after the last abortion, or until after the last application of the so-called "devitalized vaccine." This is a vaccine prepared from massive cultures of virulent and agglutinating organisms subjected to chloroform, which, according to the researches of Duval and Harris, in connexion with Pfeiffer's bacillus, "devitalizes the bacilli by rapidly absorbing the water, and in consequence increasing the permeability, which results first in plasmolysis, then rupture of the bacterial cell, liberating, without affecting in any manner, its toxic moiety." I, personally, adopt this method of vaccination in preference to the use of (1) vaccines composed of live, virulent organisms, which can only be used at the risk of causing abortion and of setting up new foci of infection; or (2) of vaccines composed of living organisms, which, as the result of many subcultivations, have lost their virulence, and, possibly, other essential antigenic properties. I also consider it preferable to the use of a vaccine composed of organisms whose toxic and other properties have been destroyed by heat. The necessity for retaining the essential properties of an organism in a vaccine has recently been emphasized by Tulloch, Davidson and others, in papers read before the British Medical Association at Bradford, and many of the principles enunciated by them have been observed in the preparation of the "devitalized vaccine." Numerous reports have been received, and continue to be received, indicating most satisfactory results following its application. Of course some abortions are inevitable, even after vaccination—life cannot be restored to a dead foetus—and, as the immunity conveyed is only temporary, much depends upon the efforts of the Veterinary Department, and of the owners, to remove the source of infection before the immunity has worn out.

The advice now given in dealing with the disease, especially in range cattle, is first to seek out and eliminate the source of infection, to disinfect cow-sheds, kraals, and watering places, to destroy non-breeding cows and those constantly returning to the bull, to test all bulls and remove reactors, and to vaccinate all females in danger of becoming infected. The present low price of cattle makes the culling of non-breeding females a feasible proposition. Owners are even urged to sacrifice any animal which, having had the opportunity of becoming pregnant, has failed to produce a calf. It is suggested that the protection of susceptible in-contact animals by vaccination should be carried out systematically, and if, by reason of the large number of females involved, this is impossible, it should be applied to the heifer herds, say, two months before the bulls are run with them, and at intervals of three months, in order that the immunity may be carried on throughout the whole period of pregnancy. This can be safely done with the "devitalized vaccine," which causes no ill-effects.

This short review of the subject will indicate that in Rhodesia the veterinary profession is fully conscious of the gravity of this disease not only as a source of loss to the cattle industry but because of its possible menace to human health, and that it is doing its best to cope with it, realizing that in this, as in so many other animal diseases communicable to man, it constitutes the first line of defence.

With regard to the measures adopted by the Public Health Department: undulant or Malta fever has been included as a notifiable infectious disease under the Public Health Act of 1914, which provides for the inspection of dairy cattle and of animals intended for human consumption, and of dairies, cow-sheds, milk shops, &c., and for the taking and examination of samples of milk and dairy produce. Under this Act the Minister may make orders "requiring the closing of any cowshed, dairy or milk shop, or the exclusion from any cowshed or dairy premises of any animal, the milk from which, there is reason to believe, has conveyed, or is liable to convey, any infectious or other disease prejudicial to public health." It will therefore be seen that every effort is being made by the authorities in Southern Rhodesia to combat this menace.

This problem, however, presents many difficulties, but is essentially one for the consideration of the Section of Comparative Medicine, in order that our two professions may collaborate in devising methods for the protection of bovine and human health.

Postscript.—Since sending my communication on the subject of infectious abortion of cattle and its possible relation to human health in Rhodesia, I have received from Messrs. Huggins and Hurworth the following description of cases of undulant fever which have been under their observation.

Undulant or Malta fever as met with in Southern Rhodesia has always been insidious in its onset. During the *initial stage*, which may last for three or four weeks, there is usually little pyrexia unless that due to other causes, such as malaria. The symptoms during the early stages are lassitude, anorexia, constipation or mild diarrhoea. Frequently, indefinite neuralgic pains first attract attention. These are sometimes severe.

All those cases under review which have entered the *pyrexia stage* have continued to run a temperature for a period varying from two to fifteen weeks. There are no recorded relapses, that is, none have shown remissions or undulations, the fever has been of a continued rather than an undulating type. In the cases reviewed no two temperature records are alike. The irregularity and departure from text-book descriptions may in some cases be due to malaria, or to the influence of drugs.

The pulse is usually rapid (between 95 to 120). The recorded symptoms, in order of frequency, have been: marked night sweats; neuralgic pains; malaise; constipation; slight diarrhoea. An interesting feature is that in cases in which only a slight temperature, e.g., 97° F. to 100° F., has been recorded, the symptoms have been most marked, whilst cases in which temperatures reached 103° F. or 104° F. were frequently only kept in hospitals with difficulty; the patients felt tolerably well, had a good appetite, and, having grown used to the temperature, had come to ignore it.

The *physical signs* of the disease, in order of frequency, have been anæmia; splenic and hepatic enlargement; tendency to cardiac dilatation with moderate tachycardia.

Complications have been few, but persons debilitated by any other disease, such as chronic bronchitis or rheumatic arthritis, have sometimes suffered from exacerbations of the "old complaint."

Arthritis, bursitis, vesiculitis (with blood-stained semen), orchitis and pyæmia have been met with.

With regard to treatment, the following drugs have been tried: emetin, quinine, arsenic, sodium salicylate and aspirin. The last two have been effective in relieving pain in some cases. With the exception of arsenic in organic form, given intravenously, which appeared to affect the temperature favourably, no claim can be made to any value in drug treatment.

Rear-Admiral Sir PERCY BASSETT-SMITH, K.C.B., C.M.G.

For many years undulant, Mediterranean or Malta fever was thought to be restricted to the Mediterranean littoral; gradually it has been traced far inland in France, Italy and Spain; has been recognized in India, Asia, Africa and America, and has now become world-wide. The causative organism was found by Bruce, and further research showed that the common source of infection was the goat, and that it was transmitted by the milk of apparently healthy animals.

In the course of the investigations into its ætiology, other animals, such as cows, mares, sheep and dogs, &c., were found to be occasionally infected. They were not believed to play any important part in the spread of the disease, though transmission through their agency was thought possible. Hence the higher ungulates have for long been known to be a potential source of infection, particularly in India. In South Africa and in America it has been to the introduction of infected goats that cases of the disease have been traced.

For many years infectious abortion in cattle and its organism *Bacillus abortus* (Bang) have been known in Europe, and though very prevalent in some places, no cases of human infection from the disease have been recognized. The work of Evans, Fleischner, Shaw and Meyer (in 1922) has aroused fresh interest. These workers demonstrated the close relationship morphologically, culturally and serologically

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between the two organisms, *Bacillus abortus* and *Micrococcus melitensis*, and various strains were separated by higher bacteriological tests. In 1923, Miss Evans, from forty-nine strains recognized seven groups, but only three important: (1) *Bacillus abortus*, almost entirely in animals; (2) a wide group including both, and (3) a smaller group of three, including the *Micrococcus melitensis* of Bruce, able to be separated from the others. Nine further strains were received from Burnet, in Tunis; these were more closely allied to the third group, that is the original Bruce type, than to the other serological groups, agreeing in some factors with the *Micrococcus paramelitensis*. Evans also was able to infect a heifer with a human strain of *Micrococcus melitensis*; this caused the animal to abort in six weeks, a common factor for both organisms.

The researches of Bevan and Orpen, in South Africa, have widened our views. These authors show that probably the cows in Rhodesia are commonly infected with *Bacillus abortus*, and that cases of an undulant type of fever are much more common there than is generally supposed (a view promulgated by Strachan years ago).

Is this human infection of bovine origin or not? Is it due to an exaltation of virulence of the *Bacillus abortus* or is the infective abortion of cattle caused by a varied strain of the *Micrococcus melitensis*? Duncan's recently published paper (1925) has given the facts, as now known, very fully; the deduction is that the cow infection is transmitted to man by an organism not separable from *Bacillus abortus*, but varying from the Mediterranean type of *Micrococcus melitensis*.

It was Kennedy, in London, who found that some cow's milk agglutinated the *Micrococcus melitensis* in three out of twenty-one tests. Following up his work I carried out the lacto-reaction in milk from cows in a dairy farm at Greenwich, and I found no positive reactions in thirty-seven samples of fresh milk at a dilution of one in twenty, but eleven with one in two after the milk had been kept twenty-four hours. This agglutination probably depends upon the amount of infection of the cows by the *Bacillus abortus*.

The serum of human cases of undulant fever from the Mediterranean, at the time under treatment at Greenwich, was found to agglutinate almost equally well both the *Micrococcus melitensis* and the *Bacillus abortus* 80. It is therefore important to decide whether this infected cow's milk has any power to produce immunity to the *melitensis* infection, if not producing the disease.

Sedgwick and others found specific agglutinins for *Bacillus abortus* in a small percentage of infants not wholly breast-fed; Fleischner, Shaw and Meyer were not able to confirm this, though they have shown that virulent strains of *Bacillus abortus* in sufficiently large doses are pathogenic to monkeys. But it takes a dose about a thousand times greater than that of the *Micrococcus melitensis* to infect them.

I have this year put up 130 different sera (taken for Wassermann tests) with *Bacillus abortus* 80, in dilutions of 1 in 40 to 1 in 1,200. In two only was there any positive reaction, and then not above 1 in 40, therefore evidence here in man of infection or immunization from milk to this organism is very small. It is interesting to learn that Khalid has been able to cross-immunize a monkey with the two organisms, and Burnet has been able to protect humans with *Bacillus abortus* from *melitensis* infection (1924), hence the possibility of protective immunization with the less dangerous organism used as a vaccine. In spite of the negative evidence of Coolidge and Edwards as to the pathogenicity to man of the *Bacillus abortus*, it seems certain that particular strains found in cows can infect the human subject and cause a type of fever like undulant, and that this is most common in Rhodesia.

In conclusion, my considered opinion is:—

(1) That when the *Micrococcus melitensis* is first obtained from a human Mediterranean case the organism is always a coccus. By culture it becomes oval, may form chains, and finally shows the bacillary type.

(2) That this original type of Bruce does differ from the *abortus* types; I cannot, however, hazard a guess where the *paramelitensis* should be placed; it certainly is more toxic in animals and shows a greater tendency to abscess formation, thus following the characters of *abortus* as described by Jaffé.

(3) That the clinical descriptions of the South African cases show some differences from the Mediterranean types, as described by Strachan.

(4) That the formation of a large number of varieties under different names, through serological differences only, is premature and confusing.

(5) That the test of pathogenicity is the most useful guide.

Colonel J. C. KENNEDY, C.B.E., M.D.

said that his observation of the presence of agglutinins for *Micrococcus melitensis* in the milk of cows in London was made in 1913. By the time it had been published in the early part of 1914 he was in India, and he regretted very much that foreign service and the war prevented his following up the observation. He wished to acknowledge the work of Colonel Lyle Cummins and his co-workers, who repeated and confirmed his (Colonel Kennedy's) experiments. It seemed likely that had he isolated *Bacillus abortus* from the cows at that time he would have called it *Micrococcus melitensis*, and that would have been unfortunate.

It would appear that the two organisms could not be differentiated by cultural or serological tests, nor indeed by their pathogenic effects on animals, except in the case of monkeys and man, *Bacillus abortus* being very slightly pathogenic for monkeys, and according to Nicolle, non-pathogenic for man. His (Colonel Kennedy's) own experience of the infection in cows was limited to Malta and to his observations in London. Cows in Malta showed specific agglutinins for *Micrococcus melitensis*, and excreted an identical organism in their milk. He did not think that any tests for pathogenicity had been carried out, so that it was quite possible that this organism was really *Bacillus abortus*. He was unable to imagine that the English strain of *Bacillus abortus* could be virulent for man. Considering that *Micrococcus melitensis* could infect through the slightest abrasion or by way of the mucous membranes, was it possible that the milkers and those who handled the milk in our dairies could escape infection? This seemed to be a very strong point against the English cow organism being the same as that of the Maltese goat.

The course of the disease in goats varied in different places; it would appear to cause a high proportion of abortions when introduced into a clean herd. In Malta, however, abortion was not the rule, and so far from the secretion of milk being diminished it seemed in some cases actually to be stimulated by the infection. This could be explained by an acquired immunity.

In offering an explanation for the high degree of virulence possessed by the goat strain for the human subject, Colonel Kennedy referred in some detail to the cross-infection between goat and man in Malta and to the fact that *Micrococcus melitensis* by repeated passages through one species of animal became highly virulent for that animal.

Referring to the clinical features he mentioned that 5 per cent. of male human subjects suffered from epididymitis and orchitis, and that, during convalescence, they were apt to suffer from emissions of blood-stained semen; also that infection of the human subject during sexual congress was possible.

He was opposed to the American view that *Micrococcus melitensis* should be classified as a bacterium. When freshly isolated from the tissues it was a coccus, and when studied in hanging-drop serum cultures grew as a coccus in the form of a streptococcus. When cultured, it might tend to assume a bacillary form just as did many of the streptococci of the throat. However, as Bang's organism was described as a bacillus, and the two organisms were obviously very closely allied, he supported the proposal to include the two organisms in a new group to be called *Brucella*.

Professor LOUISE McILROY, M.D.

Before the war I investigated the cause of abortion in women, and had formed the theory that it might in some cases be due to a specific micro-organism. I examined a number of specimens from abortions in cattle and investigated Bang's bacillus. The results, however, were negative so far as the human patient was concerned. I also investigated the condition of women who worked on farms but was unable to find a case of contagious abortion.

The question is, what organisms affect the human uterus and cause abortion? Coliform organisms and streptococci are found in women who have aborted. I believe that the majority of cases are due to contamination and not to a specific organism. I further investigated the question of epidemic abortion among women but found no proof of this except in outbreaks of epidemic diseases such as influenza in 1919, when the abortion-rate was high among patients infected with the disease. That was easily explained, as influenza is a toxæmia. Practical experience shows that a toxic condition is liable to lead to abortion. When a pregnant woman contracts scarlet fever or pneumonia she may abort.

The nearest parallel in the human subject to contagious abortion in cattle is syphilis. It may be conveyed by the male. The ovum and uterus may become infected.

Abortions in both diseases are liable, when recurrent, to take place at a later period of pregnancy successively, and finally term may be reached. The explanation probably is that immunity was gradually acquired. In syphilis there is a serum reaction, and also in contagious abortion.

Sterility is not uncommon as a result of both diseases.

It is a clinical rule that before any cause other than syphilis can be assigned for abortion a negative Wassermann reaction must be found.

I have not had experience of Malta fever, but abortion is not uncommon in malaria. This may be due to the disease or to its treatment by large doses of quinine. Abortion sometimes becomes almost a habit when once it has occurred, as the result of a sudden jolt or jar. It is difficult to prove that coli infection causes abortion directly. It is not a common infection in pregnancy of the genital tract but is more frequent in the urinary organs.

The endocrine organs no doubt exercise an effect upon the ovum first, as the ovum in itself is a temporary internal secretory organ. The effect of the administration of extract of corpus luteum or thyroid to women who suffer from recurrent abortion seems to prove this. This treatment often enables the pregnancy to go to term.

Blood grouping might prove an interesting study. The agreement of the ovum with the paternal or maternal group may influence its relationships with the maternal organism, harmonious or otherwise.

I should like to have heard something more definite about abortion among goats. Is it merely a popular superstition that when a goat is kept among a herd of cows it acts as a prophylactic agent against abortion? If goats do not abort might it be possible to use the serum of the goat as a method of preventive treatment?

Mr. LESLIE PUGH

said he had been struck by the analogy which appeared to exist between contagious abortion as it occurred in cattle, and as it existed in goats. Dubois, in 1910, before any such action was discussed, stated that when the disease appeared in the first place in a clean herd, abortion occurred in from 60 per cent. to 90 per cent. of the cases, whilst in the next generation the percentage was much reduced, and in the following generation to that, although the animals were obviously highly infected, they did not abort, and that state persisted in the herd. This seemed also the case in the herds of cows in this country. But if pregnant heifers were imported from some other

farm, then the abortion rate became very high. The analogy between Dubois' statement with regard to goats, and the experience with cows in this country, was a close one. It seemed likely that the urine of cattle might be a source of food contamination. Bang, McFadyean and Stockman held that the digestive tract was the commonest route of infection in the case of contagious abortion in cattle. Yet, it was a matter of common observation that even when cattle were isolated before the act of abortion took place, and were kept isolated till all uterine discharges ceased, it did not stop the infection spreading. It had been said in this discussion that the urine of infected goats contaminated the food supply, and he (Mr. Pugh) thought it was possible that the urine of cattle was infected before abortion took place, and that might be the explanation of abortion not being controlled in this country at the present time.

Mr. J. T. DUNCAN

referred to a case of the Rhodesian type of undulant fever which he had examined during convalescence. The patient contracted the disease at Salisbury, Rhodesia, in January, 1924, and came to England six months later. The case presented certain points of interest: First, the symptoms, temperature chart and general clinical record were very typical of a mild form of the Mediterranean disease; secondly, the patient's occupation of butcher suggested a possible mode of infection directly from the cow; lastly, the causal organism—an apparent *Bacillus abortus*—was recovered by culture from the blood when the patient had been afebrile for more than two months.

The patient's serum agglutinated the homologous bacillus in titres up to 1 in 2,500: it also agglutinated in high titre various strains of *Bacillus abortus* and *Brucella melitensis*. Cross-absorption tests were carried out with the patient's serum, a rabbit serum prepared with the Rhodesian (patient's) bacillus, and a stock *Brucella melitensis* serum. The absorbing strains used were *Brucella melitensis*,—a strain recently isolated from a Mediterranean case, *Bacillus abortus* 80, and the Rhodesian bacillus referred to. (*Brucella paramelitensis* was also used but was found to be quite distinct from the other types). All of these three strains showed close serological affinities, but whereas the Rhodesian sera from patient and rabbit could be completely exhausted of their agglutinins only by absorption with the homologous bacillus or *Bacillus abortus*, and not completely by *Brucella melitensis*, the stock *Brucella melitensis* serum could only be exhausted by *Brucella melitensis* and not completely by either the Rhodesian bacillus or *Bacillus abortus*. A *Bacillus abortus* serum from a naturally infected cow, obtained through the courtesy of the Royal Veterinary College, could, however, be exhausted by absorption with any of the three strains.

Serologically, therefore, the Rhodesian bacillus appeared to be identical with *Bacillus abortus*, and to be distinct from *Brucella melitensis*. However, in view of the fact that the American workers, Feusier and Meyer, and Miss Evans, had described races of *Brucella melitensis* serologically indistinguishable from *Bacillus abortus* but differing in this way from other races of *Brucella melitensis*, one hesitated to accept, on serological evidence alone, the identity of the Rhodesian bacillus as a true *Bacillus abortus*.

A pregnant rabbit was inoculated intravenously with three doses of a living culture of the Rhodesian bacillus. Unfortunately it was not possible to observe the animal personally, but apparently it aborted about a week after the first dose. No other animal experiments were attempted, as it had been clearly shown that in their pathogenicity for the lower animals the *abortus* and the *melitensis* types were very similar, differing only in their virulence for particular animals.

Cultural and biochemical tests offered no trustworthy means of identifying a single strain, but it was noticed that on most culture media the growth of *Bacillus*

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abortus and the Rhodesian bacillus was much more luxuriant than that of *Brucella melitensis* or *Brucella paramelitensis*. On the alkaline potato medium recommended by Meyer and Shaw the *abortus* strains and the Rhodesian bacillus yielded a thick creamy growth with no pigmentation, while the *melitensis* cultures showed a thin growth with areas of pigmentation varying from chocolate brown to black. That this test was not altogether trustworthy was proved by the behaviour of one of the *paramelitensis* strains which resembled *Brucella melitensis* in some of the cultures and *Bacillus abortus* in others.

Biochemical reactions carried out with sugars, alcohols, glucosides, starch, urea, salts of organic acids, &c., yielded no means of identifying single cultures of either type.

The effect of variations in the reaction of the medium on growth was found to be the same for both types.

The lysozyme described by Fleming did not cause lysis or inhibition of growth in any of the cultures of *Bacillus abortus*, *Brucella melitensis* or the Rhodesian bacillus.

However, although no distinctive test for either type was found, it was noticed from time to time that minor differences occurred amongst the cultures:—differences in the morphology of the organisms, of the colour or general appearance of the growth, or in the reaction of the media in which the organisms were grown. When such minor differences occurred in a set of cultures, it was always possible, without reference to the labels, to separate the cultures into two lots, one of which would be found to include all the *abortus* strains, and the other all the *melitensis* and *paramelitensis* strains. On these occasions the Rhodesian bacillus was always found amongst the *abortus* cultures. In view of this and the serological findings, he (the speaker) suggested that the Rhodesian bacillus might be accepted as a type of *Bacillus abortus* which differed from the *Bacillus abortus* (Bang) of this country in being pathogenic for man. How this property was acquired had not yet been shown. He was informed recently by a Rhodesian farmer who had himself suffered from the local type of undulant fever, that his fellow farmers believed that the abortion bacillus was introduced into Rhodesia with English pedigree stock, and that epizootic abortion there is a disease of comparatively recent origin. If this was the case, it was conceivable that the passage of the virus from the English stock, which presumably possessed some natural resistance, into the more favourable soil provided by the wholly unprotected native African cattle, might lead to an exaltation of virulence and, perhaps, the development of new pathogenic properties in the bacillus. The value of this hypothesis was, however, greatly discounted by the discovery, mentioned in the very valuable contribution made by Mr. Bevan, just read, of naturally infected cattle in remote parts of the country far removed from any possibility of infection from imported stock.

Dr. H. H. SCOTT

said that Fikai and Alessandrini had recently reported two outbreaks of disease, one of fifteen persons, who had attended an aborting cow. Among these persons the disease resembled undulant fever; the temperature, however, did not show the intermitting periods but was continuously elevated for a long time. From two of these patients Fikai and Alessandrini had succeeded in isolating the *Bacillus abortus*. This organism resembled, morphologically and culturally, the *Micrococcus melitensis*, but they found that it could be differentiated by the following serological test, namely, if the patient's serum was diluted with distilled water instead of saline in the first instance, and thereafter with normal saline, an anti-*melitensis* serum would still agglutinate its homologous organism after being heated to 60° C., but not if heated to 65° C.; on the other hand an anti-*abortus* serum would withstand this temperature and even higher temperatures. If heated to 70° C. such a serum would still retain

its agglutinating powers, though these were lost at 75° C. or over. This was a test which could be easily confirmed or refuted, and if it were found to be correct it would constitute an easy means of differentiation.

Mr. A. L. SHEATHER

said that statistics showed that in the majority of cases cows infected with contagious abortion did not abort more than once, although it was not by any means unknown that an infected cow might slip her calf twice or even three times.

He gathered from what had been said that it was thought that an infected cow invariably aborted. This, however, was not the case. A very considerable proportion of cows, proved to be infected, carried their calves to full time. This fact complicated the matter of eradication of the disease.

With regard to the specific nature of the agglutination test he (Mr. Sheather) thought that caution should be exercised. While in India, he was in close touch with a case of glanders in the human subject, and the patient's serum gave a very high reaction to the Widal test.

There was no doubt that the main source of infection in contagious abortion was derived from the cleansings and the discharge which were evacuated at the time of abortion. But it had been proved in America, in Australia and in this country that in about 30 per cent. of infected cows *Bacillus abortus* was passed into the milk. Calves fed upon such milk became infected, but the infection was only temporary, and did not appear to lead to any degree of immunity.

It had been said that when contagious abortion gained entrance to the herd the first abortions took place at an early stage of pregnancy, and subsequent abortions at progressively later stages. This statement was not borne out by statistics, which showed that the majority of abortions occurred between the sixth and the eighth months.

With regard to the old superstition that the presence of a goat on the premises prevented contagious abortion among cattle, this point was almost always brought up at lectures given to branches of the Farmers' Union, but nowadays it was almost invariably treated as a joke.

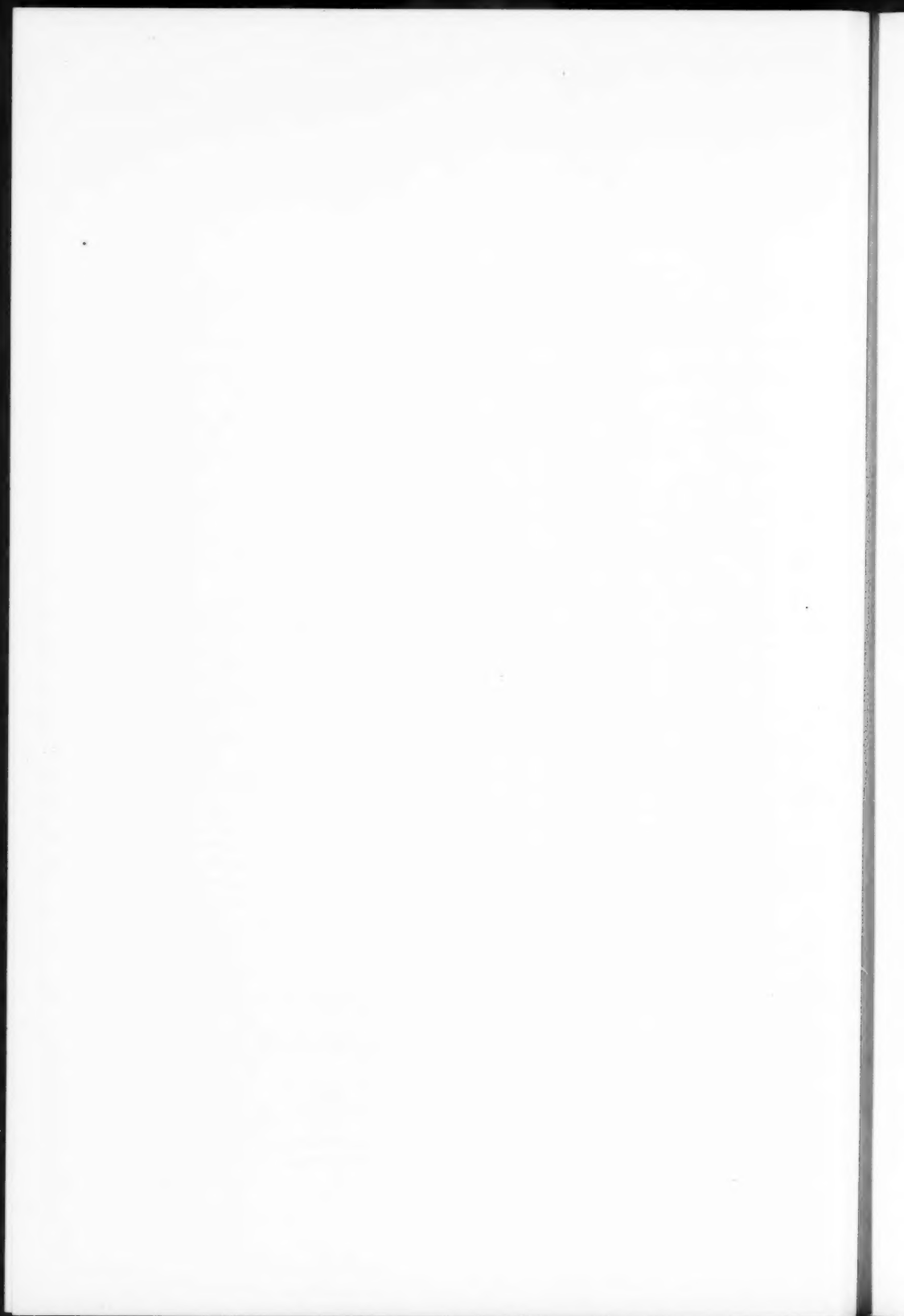
Antiserum had been tried as a prevention of contagious abortion, but without success.

Professor EYRE (in reply)

said that all appeared to be agreed that the *Micrococcus melitensis* had not yet been proved to be a bacillus; and he thought he could say that Colonel Kennedy was not likely to mistake *abortus* for *melitensis*.

He would like to know the result of blood cultures in Rhodesian undulant fever; also, he wished to know whether in cases of contagious abortion in cows, the animals excreted the organism in their urine. All the clinical information he had on the subject had been derived from books, some as recent as 1923, and he could not find any references to the examination of the urine in such cases.

The discussion had provided much food for thought, and showed that more work must be done and certain points cleared up, before a better understanding could be reached. He wished to draw attention to the tendency there was to make a diagnosis of identity upon serological grounds alone. Serological groupings were not all-important.



Sections of Balneology and Climatology, Epidemiology and State Medicine, Medicine, Therapeutics and Pharmacology.

Chairman—Dr. W. EDGECOMBE (President of the Section of Balneology and Climatology).

DISCUSSION ON THE NATURE, PREVENTION, AND TREATMENT OF FIBROSITIS.

Dr. W. EDGECOMBE.

THE title of our discussion is "The Nature, Prevention, and Treatment of Fibrositis." At the outset it is necessary to define what we mean by the term Fibrositis.

Fibrositis is an acute or chronic inflammation of the fibrous structures of the body—fasciæ, aponeuroses, intermuscular planes, ligaments, tendons and sheaths, and the subcutaneous tissues.

Anatomically and ætiologically fibrositis is bound up with arthritis. To include the latter in our discussion would be immensely to widen its range. The subject must therefore be limited strictly to the non-articular forms of the so-called "rheumatic" disorders, generically termed fibrositis, and regionally named according to the part affected: Muscular rheumatism, lumbago, torticollis, cephalodynia, pleurodynia, panniculitis, sciatica, brachialgia, and other forms of neuritis.

The various forms of fibrositis are of extremely frequent occurrence in all ranks of society. Though not a serious condition in the sense of being inimical to life, it is intensely disabling in its acute phases, and crippling to a high degree in its more chronic forms. As affording evidence of the widespread disability occasioned by non-articular "rheumatic" affections among the insured population, the report of the Ministry of Health on the Incidence of Rheumatic Diseases, issued early in 1924, may be quoted briefly. "Nearly one-sixth of the industrial invalidity of the country is due to diseases classed as 'rheumatic.' Each year these diseases are costing the Approved Societies nearly £2,000,000 in sick benefit, and the nation over 3,000,000 weeks of work from the insured population alone. Half of this loss, both of money and of time, is due to chronic joint disease."

Again—"Supposing the sample of population here taken to be a fair one, there must be approximately 56,000 cases of muscular rheumatism, 90,000 cases of lumbago, and 27,000 cases of sciatica and brachial neuritis occurring each year in the insured men in England and Wales. In addition there will be some 52,000 cases of non-articular 'rheumatic' cases amongst insured women." Add to these the numerous cases that occur in the higher walks of life, among the uninsured population, and some conception will be gained of the startling frequency of the disease and of the enormous economic loss resulting from it.

Discussion of the subject, therefore, if it point the way to more efficient treatment, preventive and curative, cannot fail to be of interest and service. It is unnecessary to consider the *symptoms* and *physical signs* of the various manifestations of fibrositis: they are well known to you all. Nor need time be spent on the *morbid anatomy* of the condition: that has been worked out by numerous investigations, and is well understood. Interest chiefly centres on the *pathogenesis*. Up to recent years these conditions were looked upon as almost entirely of metabolic origin; set up, may be, by some local cause such as a chill, over-exertion, or static strain, but due fundamentally to some underlying constitutional condition such as gout. In the ninth edition of Osler's "Medicine," published as recently as 1920, the article on

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"Fibrositis" contains no reference whatever to infection as a causative factor; there is not even a hint of such a possibility.

Of late years, however, the importance of infection in the causation of fibrositis—as of arthritis—has been fully realized, and numerous observers have established beyond all possible doubt the overwhelming part it plays as an ætiological factor. Recent text-books make abundant reference to it. To such an extent has the infective factor been stressed, that one is tempted to question whether the pendulum has not swung too far in this direction, and whether those who deny the existence of fibrositis without antecedent or present infection are not in danger of overstating their case.

Is there evidence sufficient to justify the belief that there are forms of fibrositis of purely metabolic origin, and wholly independent of infection? That, I submit, is an interesting topic for discussion.

The chief portals of infection are well known:—Oral sepsis, teeth and tonsils; nose, nasal sinuses and naso-pharynx; bowel, bladder and kidney; uterus and Fallopian tubes; gall-bladder, appendix. Septic foci that are latent, having no outlet to the surface, are more potent in giving rise to fibrositis than those having a free vent; for the contained bacteria, and their toxins, have no exit except by way of the blood-stream, through the channels of which they become disseminated throughout the body.

Are the pains of muscular rheumatism produced by the irritation of nerve endings, or by the bacterial toxins; or are they due to the actual lodgment of the organisms themselves in the capillaries and tissue spaces? That is a point of academic interest upon which opinions may be elicited.

It seems clear that there is no one specific organism responsible for the production of fibrositis. As severe muscular pains may be produced through acute infection by widely different organisms—as in the pains of influenza, or the intense "backache" of small-pox—so the pains of fibrositis may be set up as acute or chronic infections by organisms of various types. Infection by any specific organism—as in typhoid, dysentery or gonorrhoea—may give rise to fibrositis. The types of bacteria found normally in health as parasites on the mucous surfaces and on the skin may each and all become effective as causes of fibrositis when general or local loss of resistance permits their entry, or that of their toxins, into the body. Streptococci of various types are far more common as causal agents than other organisms; and of this large group the various strains of *viridans* are most frequently met with. The *Streptococcus faecalis*, *Streptococcus salivarius*, *Streptococcus mutans*, *Streptococcus zymogenes*, may each be found in different cases. The coliform group and the staphylococci are less common as causes of fibrositis.

An interesting point is the selective affinity of different types or strains of organisms for different tissues, as suggested by Rosenow. Is there any evidence known to those present tending to substantiate this attractive hypothesis?

Granted that infection by micro-organisms is the dominating factor in the production of fibrositis, there remains to be considered the soil on which the infection falls. It is well known that many people harbour foci of infection without suffering from "rheumatic" manifestations. Only when something occurs to break down their resistance or lessen their immunity do they become affected. Others, again, are notoriously prone to frequent manifestations of fibrositis, and we are accustomed to regard these persons as victims of the gouty diathesis.

In these cases, is the nature of the soil so changed by the underlying metabolic disturbance, gouty or otherwise, as to render them less resistant to infection, even to organisms of a low grade of virulence? Or can the underlying metabolic disturbance give rise to fibrositis of purely chemical origin in the absence of bacterial infection? In short, is there a purely metabolic as opposed to a purely bacterial origin of fibrositis?

To prove definitely the purely chemical origin is difficult. It is not easy to

eliminate with certainty all possible sources of latent infection. It is certain, however, that there are cases in which no source of infection can be found, and which recover under treatment directed solely to rectification of their faulty metabolism. Further, some cases with a definite septic infection, treated and eradicated on modern lines, may fail to show the improvement expected, until the nature of the "soil" has been altered by treatment of the underlying metabolic derangement.

The disturbances of metabolism with which fibrositis is most commonly associated are:—(1) The gouty state; (2) that produced by dietetic errors; excess of carbohydrate foodstuffs combined with too little exercise; (3) hyperglycæmia as in glycosuria and true diabetes.

The frequent association of fibrositis and neuritis with hyperglycæmia lends support to the view that chemical changes alone are competent to give rise to the condition; unless we are to suppose that in all such cases there is the factor of mild infection always present. The point is of cardinal importance, for if the metabolic origin be denied, and the bacterial origin be regarded as universal, then treatment on any other than anti-infective lines becomes of little use in effecting a permanent cure.

On the predisposing and exciting causes it is unnecessary to dwell. Damp, cold climate, and environment; chill; occupations involving exposure to extremes of temperature; over-exertion; sedentary living and overfeeding; all are well recognized.

The treatment may be discussed from the points of view of prevention and of cure.

(1) *Preventive treatment* aimed at the reduction of the immense mass of disease and invalidity among the insured population should embrace: (a) the better housing of industrial workers; avoidance of damp houses; abolition of slum areas, and cellar dwellings; provision of better ventilation, and more sunlight; (b) the improvement of the conditions under which industrial workers labour; avoidance of chill; provision of baths and drying rooms at collieries, mills, factories, and other places of employment; (c) the eradication of common sources of septic infection, as from tonsils or teeth.

(2) *Curative treatment* of the individual includes general measures, and local means to relieve pain and disability.

(3) *General treatment* comprises (a) the detection and removal, when possible, of any source of septic infection; (b) where no signs of infection can be found, treatment of the underlying metabolic derangement; (c) even when a focus of infection has been definitely established, treatment of the underlying predisposing cause is usually necessary.

Into the details of (4) *local treatment* it is unnecessary to go. The multifarious methods available must be varied according to the stage of the condition, whether acute or chronic; according to the seat of the disease, and according to the individual needs of each patient. They are all well known to you.

In cases where infection is definitely present—and too often when it has not with certainty been found—vaccine treatment is largely used. In my experience the results, though striking in a few cases, are disappointing in the majority; and especially is this so in the more chronic forms of fibrositis when vaccine treatment is used alone without other measures. The reason is not far to seek. When definite patches or nodules of induration have formed in chronic cases, unless something is done to improve the blood-supply to the affected parts, presumably foci of infection, the antibodies formed in the blood by the stimulus of the vaccine cannot reach the spot and therefore fail in their effect.

Do the methods comprised under the comprehensive term "spa treatment" offer any advantages in the management of these cases over ordinary medical means available at home? The principles of spa treatment, shortly stated, are: the alteration of the metabolism of the patient in the anabolic or katabolic direction,

according to the needs of the case; the regulation of the intake of food; the promotion of the output of waste products by the bowel, kidneys, and skin; and the improvement of body nutrition by alteration of the interchange of tissue fluid effected by changes induced in the circulation by means of physical methods and various balneological procedures. These principles are especially applicable to the class of case we have under consideration. Such methods are not usually available at home, and are to be found in their entirety at any well-equipped spa.

Though open to the well-to-do patient and to those of moderate means, spa treatment is less available to the industrial population. It is worthy of serious consideration by the Ministry of Health, and by the Approved Societies collectively or individually, whether a great economic saving could not be effected by the more extended use of the spas in the treatment of their members disabled by fibrositis in its various forms. True, many cases are already sent to the three great mineral water hospitals at Bath, Buxton, and Harrogate; but these provide for the merest fraction of the whole. The experiment would be well worth trying, on a large scale, of sending a series of cases, say of lumbago or sciatica, for institutional treatment to one or other of the spas, and comparing the results with an equal number of similar cases, as controls, treated, as at present, in their home surroundings. I venture to think that the trial would speedily demonstrate that a great economic saving could be effected.

In conclusion I submit to you the following points for discussion:—

- (1) Is there a purely metabolic origin of fibrositis apart from infection?
- (2) In the infective cases, what are the commonest sites of infection; what are the commonest organisms met with; is there any evidence of selective affinity of the particular organisms for particular tissues?
- (3) What is the value of vaccine treatment, alone or combined? What is its utility in chronic cases?
- (4) What means can be taken to lessen the incidence of fibrositis among industrial workers, and to accelerate their recovery?
- (5) What is the value of spa treatment as compared with other methods?

Dr. J. A. GLOVER.

It has fallen to my lot to examine and correlate the findings of some forty-nine practitioners who voluntarily acted as observers for the Ministry of Health, and who, during the year 1922, specially investigated a population of 92,000 insured persons for the incidence of the so-called rheumatic diseases, of which fibrositis is one. These findings were all embodied in No. 23 of the Ministry's Reports, and I propose to sketch briefly such of them as are interesting in connexion with fibrositis.

FREQUENCY.

Fibrositis is a common disease. Our sample population included 58,000 insured males of all ages over 16. Among these males there were in one year 1,119 cases of fibrositis, half of which (584) were cases of lumbago; one-third (363) were cases of muscular rheumatism, other than lumbago; and nearly one-sixth (172) were cases of sciatica or brachial neuritis.

The sample population of 33,000 insured females produced in one year only 376 cases of fibrositis, only 95 (one-quarter) of which were cases of lumbago; only 46 (one-eighth) cases of sciatica or brachial neuritis; the remainder, 235, being cases of muscular rheumatism.

AGE AND SEX.

As regards age, it has been a matter of common knowledge from man's earliest days that muscles and sinews, as well as joints, become stiff as age advances, and poet and statistician are for once in agreement. It will be seen from Table I how rapidly in both sexes the attack-rate increases with age.

TABLE I.
Fibrositis (all forms).

Annual attack-rate per 1,000 insured persons in each age-group.														
Age-group:—16 to 24		25 to 34		35 to 44		45 to 54		55 to 64		Over 65		Per 1,000 all ages		
Men	...	5	...	11	...	22	...	32	...	42	...	63	...	19
Women	...	5	...	9	...	16	...	31	...	36	...	*	...	12

* Omitted owing to small numbers at risk.

From Table I we see that the incidence of all forms of fibrositis is upon the whole fairly equal for both sexes. When, however, we split it up into the components, lumbago, &c., we find considerable variation.

TABLE II.
Annual attack-rate per 1,000 insured persons in each age-group.
Muscular rheumatism, i.e., excluding lumbago and sciatica.

Age-group—16 to 24		25 to 34		35 to 44		45 to 54		55 to 64		Over 65	All ages		
Men	...	3	...	4	...	7	...	9	...	11	...	23	6
Women	...	4	...	6	...	10	...	16	...	18	...	—	7
<i>Muscular rheumatism, including lumbago.</i>													
Men	...	5	...	10	...	19	...	27	...	33	...	47	16
Women	...	5	...	8	...	14	...	27	...	30	...	—	10

Muscular rheumatism, including lumbago.

For muscular rheumatism, excluding lumbago, it is seen that the female attack-rate is considerably greater than the male in every age-group. This is contrary to the generally accepted belief that muscular rheumatism is much more common in men; some authorities have indeed said three times as common.

For lumbago the generally accepted belief is upheld, the male attack-rate being far greater at all ages than the female. In the youngest group it is more than double, in the 25 to 34 group exactly three times, in the 35 to 44 group more than three times as great as the female, over middle age it is nearly twice the female attack-rate.

TABLE III.
Annual attack-rate per 1,000 insured persons in each age-group.

Lumbago.														
Age-group :-16 to 24				25 to 34		35 to 44		45 to 54		55 to 64		Over 65		All ages
Men	...	2	...	6	...	12	...	18	...	22	...	24	...	10
Women	...	1	...	2	...	4	...	11	...	12	...	—	...	3
Sciatica.														
Men	...	0.1	...	1.2	...	2	...	4	...	6	...	14	...	2.4
Women	...	0.1	...	0.3	...	1	...	1	...	5	...	—	...	0.6
Brachial Neuritis.														
Men	...	0.06	...	0.06	...	0.5	...	1	...	2	...	1	...	0.5
Women	...	0.3	...	0.5	...	1.5	...	4	...	1	...	—	...	0.8

For sciatica and brachial neuritis together generally the male attack-rate is substantially higher than the female, the difference being entirely due to the male liability to sciatica. It may be observed here that for sciatica alone the ratio of male to female cases is almost exactly the 4 to 1 ratio given by Gowers, which, he adds, forms a remarkable contrast to the analogous affection of the arm. For the latter, the attack-rate for males for all ages proved in the present inquiry to stand to the female attack-rate as 0.5 to 0.8 or very nearly as 2 is to 3.

The comparative absence of lumbago in women may partly no doubt be explained by the smaller occupational stress experienced by women on the lumbar muscles, and a similar explanation may perhaps account for the heavier relative incidence of sciatica on men, but it is difficult to see why women should suffer more than men from brachial neuritis—possibly dress is to blame.

COMPARISON WITH OTHER NATIONS.

The statistics of the Leipzig Federation of Sickness Funds, which were compiled during the twenty years ended 1907, seem to show that the attack rates I have just given are not high, in fact the comparison might be used as showing that things have much improved between 1907 and 1922, possibly owing to the recent attention which has been devoted to dental and oral hygiene in school children and others. The Leipzig trades, however, include many printing, textile and building workers, and possibly this occupational factor may explain some of the balance apparently so much in our favour.

TABLE IV.

Muscular Rheumatism, Lumbago and Sciatica.

England and Wales Inquiry. (Ordinary type.) Compared with Leipzig Statistics. (Italics.)

	MALES						FEMALES					
	16 to 24	25 to 34	35 to 44	45 to 54	55 to 64	Over 65	16 to 24	25 to 34	35 to 44	45 to 54	55 to 64	Over 65
Attack rates per 1,000 insured workers.	18.7	31.7	46.5	60.3	68.4	63.3	11.0	22.2	39.7	51.6	54.7	69.7
Practitioners	4.9	10.9	22.3	32.4	41.9	62.5	5.1	8.5	15.9	31.2	35.7	64.7
Days of sickness per annum per 1,000 insured workers.	265	516	827	1,209	1,786	2,690	213	458	856	1,272	1,501	2,901
Practitioners	47	128	318	745	1,474	5,934	81	88	515	1,071	2,516	7,899
Mean number of days of sick absence per attack. Practitioners	14	16	18	20	26	32	19	21	22	25	27	30
	9	12	14	23	35	95	16	10	32	34	70	122

Most of the recent American statistics are unfortunately compiled on lines which render them useless for comparison with our figures.

LOCAL DIFFERENCES.

Fibrositis, like osteo-arthritis, seems particularly common in the industrial towns of South Lancashire, the attack-rate being in this district 143, lumbago especially being in excess if the attack-rate for England and Wales be taken as = 100.

OCCUPATION.

The most outstanding feature in the occupational distribution amongst the males was the large number of metal workers suffering from fibrositis. This excess was almost equally prominent in the number of cases of muscular rheumatism, lumbago and sciatica as well as in cases of acute and subacute articular rheumatism. Miners, on the other hand, though in marked excess in the subacute rheumatism category, showed no excess in muscular rheumatism, lumbago or sciatica.

ÆTIOLOGICAL FACTORS.

Few will deny the importance of *chill* in the production of fibrositis, especially of lumbago; and I vividly recall the ætiological factor of local chill following upon dental sepsis in my own first attack of lumbago at the age of 26.

Strain is of great importance, too, but it is a factor particularly difficult to assess. The pain of fibrositis is usually only evoked by movement, and hence the factor of strain or violent movement is peculiarly liable to be over-emphasized.

In dental sepsis we have an ætiological factor of the highest importance. In no other disease is the explanation—the first cause—so likely to be found in dental sepsis, usually apical. This is particularly true of lumbago. Dental sepsis in my view lays the train, and chill as a rule fires it.

Tonsillar sepsis did not appear, in the series, to be a factor of importance in the production of fibrositis compared with its importance in acute or subacute rheumatism. Whilst inquiring into an outbreak of pneumonia and influenza in Sheffield in December, 1921, I was struck by the general report of an accompanying epidemic of lumbago which seemed to be well authenticated, and not to be merely due to cases of the backache of masked influenza.

Lead poisoning may be an occupational factor of importance in some cases. A considerable proportion (13 per cent. according to Goadby) of cases of lead poisoning show signs of rheumatic manifestation closely resembling muscular rheumatism.

Three per cent. of the cases of fibrositis (3·3 in lumbago, 5·3 in sciatica and brachial neuritis) gave a history of close occupational contact with lead—not a very conclusive figure compared, for example, with gout, where 11 per cent. of the male patients gave a similar history.

PREVENTION.

As to the prevention of fibrositis much can be done. The school dental service is an immense step forward, and no opportunity should be lost of preaching and practising dental hygiene to every age and every class. Super-taxpayers with gold crowns sitting upon dead roots need education as much as anyone.

Increased dental treatment for adults is a prime necessity.

First aid for minor sepsis, particularly the provision of iodine and dressings in many occupations, would be of value in the prevention of fibrositis as it has been found to be in the prevention of such industrial diseases as "beat knee."

The avoidance of chill can be largely accomplished by the provision of pithead and works baths and drying rooms, and by the use of special working clothes.

SIR WILLIAM WILLCOX, K.C.I.E.

I will first say a few words in reference to the reality of fibrositis. I remember speaking here at a discussion four years ago, when upon the mention of the word "fibrositis" a broad smile passed round the room; evidently many of those present thought it was a fictitious disease. But recent work has shown, by actual microscopical and histological examination, that the co-existence of a chronic inflammation in the tissues can readily be demonstrated. Stockman gives a good account of this in his book.¹ The lumps and thickenings felt by the skilled masseur in parts of the body which are affected by fibrositis have an actual existence, and, if need be, its presence can be demonstrated by excision of a portion of the local lesion present.

Another method of diagnosing fibrositis is by radiographic examination. In France a good deal more attention has been paid to this aspect than in this country, and I here exhibit, through the kindness of Dr. Higgins, some radiographs which were taken by Dr. Gasto of St. Louis Hospital, Paris, which show around the dorsal and cervical vertebrae a deep shadow caused by the deposit in a severe case of fibrositis. I have photographs of the thighs of the same patient, one thigh being affected by fibrositis, the other not.

In cases of bacillary dysentery, acute fibrositis often develops in tendons and ligaments, and I saw many of these cases during the war in Mesopotamia and the Dardanelles. Also, gonorrhœal infection produces very striking examples of fibrositis; thickenings in the ligaments and fibrous tissues may frequently be felt. One of the most severe instances of fibrositis I ever saw was in a case of glanders. A colleague was infected while working with this organism, and he lingered on for many months, suffering most severely from the fibrositis which resulted.

¹ Stockman, "Rheumatism and Arthritis," 1922.

We shall agree with our Chairman (Dr. Edgecombe) that fibrositis and arthritis are diseases of similar etiology and causation. It is well known that fibrositis results from a number of specific infections, such as gonorrhoea, bacillary dysentery and so on, the diseases including Malta fever, pneumococcal infections, the enteric group of diseases, scarlet fever, tuberculosis, syphilis, &c.

In this discussion we are specially concerned with the forms in which the infective cause is non-specific in origin, and these include the great mass of the cases of fibrositis. Histological investigations show a chronic inflammatory condition of the fibrous tissue, with very little leucocytic exudation. Bacteriological investigations are almost always negative.

Dr. Edgecombe asks: Is fibrositis always due to bacterial infection? One is bound to agree that metabolic conditions such as gout, and toxic conditions such as lead poisoning, are commonly associated with fibrositis; but the view I am inclined to take is that in such there is also a superadded infection. In most cases of gout there is evidence of intestinal toxæmia and stasis; often there is an excess of indican in the urine; and examination of the fæces, or of the colon washings, reveals a preponderance of the organisms so frequently associated with fibrositis-streptococci, especially of the *viridans* group.

We shall all agree in assigning to focal sepsis a very important place among the causes of fibrositis, there being some centre of infection from which the toxins, or possibly the organisms themselves, are distributed through the body. We do not realize how far advanced we are in this country in our appreciation of the part played by focal infections. A study of continental medical literature, or visits to hospitals abroad, show that there focal infection as a cause of disease is only in the infancy of its recognition. One saw glaring sepsis in cases of fibrositis, and when the causal connexion was suggested, the eminent physician in charge shrugged his shoulders.

Often very careful search is needed to find the focus of infection; still, it is comparatively rare *not* to be able to discover a focus of infection if the search has been thorough and exhaustive. A focus of infection which is sometimes missed is antral infection. During the last four years I have had at least twenty cases of arthritis or fibrositis in which every other examination gave negative results, but an X-ray examination disclosed an opaque maxillary antrum, and the antrum was found to be filled with pus or it was infected; and the treatment of this antral condition has usually been followed by rapid and progressive improvement. I mentioned this to Dr. Monod, of Vichy, a year ago, when he was going round my wards at St. Mary's Hospital; he told me last August, when I was at Vichy, that he had since been on the look-out for cases of antral infection, and that he had met with twenty cases.

Another cause in elderly people is diverticulitis.

It is important to realize that a focal infection exists and acts as such for a certain time, but it will not be long before secondary infections follow. The colon and tonsils may be infected; there is lymphoid tissue not only in the tonsils but also scattered through the pharynx and various parts of the body, and the lymphoid follicles may be infected. Therefore a secondary infection may be carried on without any very gross obvious visible focus. Perhaps bacterial investigation will be the only means of proving this.

Why should the fibrositis lesions be sterile? Is it because organisms go to them and are destroyed by the fluids of the body? Or is it because the lesions are produced by the chemical toxins carried from the focus of infection? I think the second is probably the true explanation. We know from the work of Dr. Gye and Dr. Kettle that colloidal silica can produce marked changes including excess of fibrous tissue in the body, and what chemical irritants may do it is reasonable to think that the toxins of pathogenic microbes may do also.

Recently I have had two interesting examples of a condition allied to fibrositis due to infection. A little time ago a case of pneumonia on the right side was followed by empyema, and then pericarditis developed. There was an infection of *Streptococcus hæmolyticus* in the pleural cavity. Mr. Waugh operated and opened the pericardium. It was found to contain a sterile, turbid fluid. There was a marked sero-fibrinous pericarditis but no organisms were present.

A few weeks ago I saw a case in which there was sterile clear fluid in the chest, due to a right-sided pyosalpynx. The patient made a good recovery after the pyosalpynx had been removed by operation. I think that a similar condition is associated with fibrositis; toxins are carried from the focus and cause the inflammatory lesions.

Fibrositis is a gauge which measures the balance between the infection and the immunity of the patient. Normally, a certain amount of absorption of toxins of bacterial origin may be constantly taking place. And I would call your attention to factors which are insufficiently realized to-day in regard to toxæmic diseases. One is the condition which is known as sensitization. Sometimes a patient suffering from an infection has been dosed daily with a poison and had, so to speak, such "knock-down blows" that he cannot rise again and has become sensitized to the infection. That is a condition which one often sees in these severe cases of fibrositis. Gout is an example of sensitization. If you take a case of gout due to streptococcal infection and you make a vaccine, in most of the cases you find that the patient is so sensitive to the vaccine that if you give only 1,000 or 2,000 organisms you bring on an attack of gout. The same applies to asthma, angio-neurotic œdema and so on. That is a factor to be borne in mind in treating cases of fibrositis and it is an explanation of the failure of vaccines in the treatment of these cases to which our Chairman has alluded. In many of the cases the reason why the vaccines fail is that the patient has become sensitized.

Another important factor is symbiosis; there is disease caused through infection by one organism, and it lowers the resistance of the body to the organism which is causing the fibrositis. This is seen excellently in people who have become infected with malaria. If the malaria is cured, they can put up a fight against the *Streptococcus viridans*, and a cure of the fibrositis follows. It applies also to dental sepsis, where a malarial infection is difficult to cure until the dental sepsis has been removed. It must be realized that fibrositis is in most cases an evidence of a streptococcal toxæmia. I do not regard fibrositis as a disease but as a symptom of toxæmia. One can find in most of these cases of fibrositis general evidence of a toxæmia. Some patients are anæmic and debilitated and show dilatation of the heart, and many suffered from other conditions, such as appendicitis, gastric ulcers, or colitis.

As regards the prevention of fibrositis, this has been dealt with by our Chairman and by Dr. Glover, and I agree with everything they have said. We have to consider those measures which will improve the health and the resistance of the individual; such as housing, good food, pure air, pure water, personal hygiene and the measures which are directed towards preventing the development of focal sepsis.

We must educate the public, though they are not yet ready for it. What is needed is periodical medical inspection by people skilled in the detection of focal sepsis. If the school examination system could be extended to every person, the early development of focal sepsis would be recognized and eradicated and the health of the community would enormously improve. I will say, in the presence of Dr. Glover, who is representing the Ministry of Health, that there is no field in the department of public health which will be productive of a richer harvest than this field of the prevention, recognition and eradication of focal sepsis. Most of the diseases I see in people over 40 years of age are due to some focal infection, and I am here, of course, leaving out such diseases as cancer. In this preventive treatment one must aim at potential health. We must not be satisfied because a patient looks

30 Willcox—Midclton: *Nature, Prevention, and Treatment of Fibrositis*

well; he may look well and yet have apical abscesses in his teeth or infected tonsils. A person should be overhauled to see whether, though apparently well, he has the seeds of disease already within him.

With regard to the treatment of fibrositis, it is most important to find the cause. The cause of fibrositis can only be found by the most careful and elaborate search, and in some regions it is necessary for the specialist to make it. Bacteriological examination of stools, urine, &c., is valuable, and one often finds that the *Streptococcus viridans* is the cause of the trouble.

Of course, the first step in treatment is removal of the focal infection or its amelioration. For instance, in intestinal trouble, Plombières treatment is desirable.

With regard to vaccine treatment, I strongly deprecate the use of vaccines in fibrositis unless the focus of infection has first been completely removed. Then vaccines can be used. One meets with cases of fibrositis sometimes in which there is sensitization, and in those cases vaccines are likely to do harm. If a vaccine is prepared it is well that the organisms for it shall be taken not only from the teeth and tonsils but also from the intestines. And may I utter a caution against over-dosage? Vaccines are a help in selected cases, but, as I say, the focus of infection must be removed.

With regard to medicinal treatment, intestinal disinfectants are a help. I frequently give carbonate of guaiacol 10 gr., three times a day, and sometimes iodine in the form of a French tincture is useful. But in the treatment of fibrositis we cannot place very great reliance on drugs.

Local treatment is of value, such as electricity, poulticing, heat, &c. Of all the treatments, apart from the eradication of focal sepsis, skilled massage by one who knows his anatomy and physiology is one of the most valuable forms. By this means the lymph movements are assisted and fresh fluid laden with bactericidal substances is brought to the affected part. In advocating massage I am referring to chronic cases. In France lipiodol has been used as a local injection in severe cases of fibrositis. Dr. Higgins can speak with greater knowledge than I possess on this subject myself.

Anaphylactic treatment such as the injection of typhoid vaccine, peptone, &c., has been used in fibrositis. I have not seen good results from this method and I do not think it is scientifically sound, therefore I do not advise it.

[March 5, 1925.]

Dr. W. J. MIDELTON (Bournemouth)

said he deprecated the number of labels at present attached to these associated conditions. These were puzzling and misleading; almost the only "label" needed was "toxæmia; chronic or acute." He (Dr. Midelton) had no faith in all that was said about staphylococci and streptococci. In all cases, he believed, the underlying condition was some result of an earlier infection—measles, scarlet fever, typhoid, and so forth—and the staphylococcal and streptococcal infections were purely secondary. One of his theories was "once infected, always infected."

[Dr. Midelton described and showed photographs illustrating the treatment for the fibrous lesions, introduced by Dr. P. W. Latham, a treatment from which he had obtained good results.]

He agreed with previous speakers who emphasized the importance of septic foci, but he was surprised that so little mention had been made of miliary foci—such as were seen in tuberculosis—or of the fact that septic foci often existed but were overlooked by some who searched for them. In one instance about a salt-spoonful of "cheesy" pus had remained concealed behind a curtain that had formed between the soft palate and the tonsil. This had been overlooked by two throat

specialists but was discovered by a third, who used a hook during his examination. He (Dr. Middelton) agreed with Dr. Watson-Williams, of Bristol, that it was impossible to discover early infection of the nasal sinuses without boring into them.

Dr. H. A. ELLIS

said that up to the present stage of the debate one might imagine that there was nothing in fibrositis but a septic condition; this was only partially true. There were a large number of cases in which it was almost or quite impossible to prove the occurrence of sepsis; and many of the difficulties of the situation would be met by a consideration of the matter from a biochemical aspect, in contrast with the purely bacterial point of view.

In the class of case which he personally had had special opportunities of investigating, he always asked whether teeth, appendix or tonsils had been removed, and if the reply was in the affirmative he then asked whether the patient felt better for the removal; the patient often replied that he did not. The patient perhaps had also received injections of various kinds, and yet he remained in the same condition.

A significant point was that the sex incidence differed, and that was very difficult to understand on a purely bacterial basis. There must be some basis which was not bacterial. So far, his (the speaker's) conclusion was that it was a biochemical condition activated by many causes, of which bacterial invasion was undoubtedly one, but by no means the sole one. As a simple illustration, it was known that one could drink port and bring on lumbago, which formed part of the subject under discussion. Did anyone suggest that this process of producing lumbago was bacterial? If so, let bacteriologists come to the rescue and give something which could be taken to counteract this effect of port. If that could not be done, those who advanced the bacterial view must prove their case.

He believed that fibrositis, like rheumatoid arthritis, fell under two main groups: one in which the activating cause was error of assimilation, and the other in which it was error of elimination. The cases in the first group were those in which, from some cause or other, the body was receiving insufficient nourishment and which he termed alkaline cases or metabolic deficiency cases. In the days when these patients were deprived of nourishment which was thought to be to their detriment, they did badly. He (Dr. Ellis) had been interested in hearing Sir William Willcox say that in addition to measures for combating bacterial invasion the patient should have good food, fresh air, as much sunlight as possible, and those other essentials upon which one relied for rectifying assimilation defects. In the assimilation error cases, the patients were naturally thin people, with long ribs and high palates, in other words, vital deficiency cases, and in that group there were many more women than men. Patients with lumbago and sciatica were elimination cases and he would term them metabolic excess or acid cases. If the same treatment were adopted for both classes, difficulties would be experienced. The reason why the second group—elimination errors—became more common with the advance of age, was the increasing difficulty of elimination, and this metabolic error would in itself produce the symptoms of fibrositis, apart from any bacterial invasion. These cases were due to the deposition of improperly metabolized material, either because the kidneys could not get rid of it, or because the heart was working at a disadvantage. This deposition might also be, as was known, produced by overwork or overfeeding, and either would cause an excess of acids in the organism, from which it was easily understood that fibrositis in the muscles might occur.¹

John Hunter, an Australian, who recently died at the age of 26, put forward the proposition that in ordinary muscle there were two types of fibres; one type which

¹ A third variety of case has been differentiated by urinary examination. This has characteristics of both varieties, acid and alkali urines being present in different specimens, and, in addition, uric acid excess is present. It is by far the most difficult type to treat.—H.A.E.

raised the arm, the other which maintained it in that position. The importance of that supposition consisted in the fact that it was the sympathetic which innervated the fibres that maintained the arm after raising. If an investigation was made into many fibrositic cases they would find that it was not the muscular movement which produced the pain, but that pain was felt when the limbs came to rest,—a fact suggesting that the sympathetic was largely involved. This gave an idea of the line along which investigation should travel.

The examination of many urines had taught him (Dr. Ellis) that there was another factor of great importance which acted throughout, whether one was dealing with metabolic excess or with metabolic deficiency. There was always an excess of magnesium excreted in the urine; usually the calcium was not materially changed, but the magnesium was increased in these cases to from three to fifteen times the normal quantity. There were, however, other conditions in which excess of magnesium was produced, therefore he could not say that all cases in which this excess was found were rheumatic.

What he had said was of great importance in treatment, for assimilation deficiency cases must be treated with acid, phosphoric acid being the best form as it was often almost entirely absent from the urine. It was largely instrumental in eliminating the pain at night. On the other hand, the large-chested, robust patients who had lumbago and sciatica must be treated with potash and alkalies. Tribasic potash he had found to be the most efficient treatment. Elimination error cases also derived much benefit from flushings out with water.

DR. OLIVER HEATH

said that, as a bacteriologist, he protested against the use in the present connexion of the terms "toxin" and "toxæmia." Such terms indicated to him something definite, like the "toxin" of the diphtheria bacillus, but no one had obtained anything of this nature from the common micro-organisms, mostly cocci, which caused sepsis, and any hypothesis based on this idea seemed to him to rest on a very shaky foundation. He described two personal experiences as a sufferer from acute lumbago with fever. Various simple treatments were tried. In the first case, following three days after a gumboil, rest or walking proved ineffective, but massage—with the object of increasing the local blood- and lymph-flow through the depth of the affected muscles—first applied with the lightest touch, then with increased pressure but avoiding pain, dissipated the lumbagic pain in fifteen minutes and the fever in about four hours. The second attack occurred as the terminal phase of an experimental fever produced in himself by injection of 500 million typhoid vaccine into a vein. Subsequent experiments he had published showed that his (the speaker's) total amount of normal blood would dissolve 400 million typhoid bacilli, and the 100 million survivors seemed to have settled in his lumbar muscles, since on the second day, as the acute fever subsided, lumbago developed. This happened while he was at rest in bed. Treatment was confined to frequent slow bending forward of the body as if to pick up an object from the ground, straightening up again as soon as pain increased. This method cured the pain in from one to two hours, and the temperature became normal in about six hours. During the fourteen years since the first attack he had used this exercise to abort threatened attacks with complete success (except for the injection experiment), and he thought this effect of exercise on lumbago might explain why working-class women suffered from lumbago less often than did working-class men as had been shown by Dr. Glover's statistics.

MR. J. E. R. McDONAGH, F.R.C.S.

considering the subject as it affects people in the different decades of life said:—Fibrositis in children is one of the manifestations of rheumatism and is most probably caused by a streptococcus. The danger in these cases is the risk of

developing endocarditis. In young adult women a focal infection is the most common cause of fibrositis and the focus is generally to be found in the tonsils, teeth, or intestines. The gonococcus is not so common a cause in these cases as it is in the case of young adult men. The peculiarity of gonococcal fibrositis is that it is much more commonly a manifestation of a recurrent attack than of the initial infection. This accounts for the cause of the condition being frequently missed, and for the fact that some other organism—the organism of dysentery for example—is wrongly taken to be the aetiological factor. Women at the menopause are liable to a form of fibrositis associated with a mild arthritis of the knees and terminal phalanges of the fingers. These patients often exhibit some degree of hyperpiesis. In the majority of cases the prognosis is good and the condition does not advance to one of generalized osteo-arthritis. The corresponding condition in men is the so-called "gouty" fibrositis. Gout is not a disease *sui generis*, but merely an inflammatory condition occasioned by the arrest of the protein particles in the plasma, in the dilated capillaries of a structure the resistance of which has been lowered by the deposition of uric acid. The actual cause of the inflammatory lesion, which should be regarded as a recurrence, is not by any means the same as that which occasioned the protein particles to deposit their liberated uric acid in the first instance. Still more does this apply to the fibrositis met with in elderly people. This form of fibrositis is the result of chronic protein dehydration. The lesion presented is often the result of the action of the dehydrator and is not necessarily a sign of its present activity. It is impossible to suggest the nature of the original dehydrator and possibly there has been more than one at work. The streptococcal fibrositis of children should be treated with sup. 468. Five injections should be made intramuscularly on alternate days, each of 0.001 gm. In young adults the focal lesion should be searched for and removed when found. In these cases of fibrositis a combination of contramine with vaccines is called for. Should an attack of fibrositis complicate an original gonococcal infection, the best treatment is to inject intravenously 0.01 gm. sum. 36 on two occasions at three days' interval. Climacteric fibrositis is combated best with thiol-histamine. Three injections each of 0.002 gm. should be made intramuscularly on three successive days. In addition iodine, thyroid and ovarian extract should be prescribed internally. Gouty fibrositis responds best to contramine injected intramuscularly in three 0.25–0.5 gm. doses at five to seven-day intervals. In very acute cases it is best to precede the contramine with 0.01 gm. sup. 36. Contramine is the drug of choice in old chronic fibrositis, but should it fail recourse should be had to injections of either insulin or milk.

Dr. M. B. RAY.

The application of the term "fibrositis" to those ill-defined conditions grouped for years under the adjective "rheumatic" is a sure indication of a more thorough understanding of the anatomical sites involved and has the additional advantage of being strictly non-committal as to the underlying causes. Although the term has been in use for a considerable time it seemed to gain a more general acceptance after the appearance of Llewellyn and Basset Jones's book on "Fibrositis," and no doubt the need for a more precise diagnosis of a number of war disabilities attributed to "rheumatism" served to fix it more firmly in the minds of the profession.

According to Stockman's excellent description of the anatomical changes: '—

The condition may be defined as one of chronic inflammation of the white fibrous tissue of the fasciæ, aponeuroses, sheaths of muscles and nerves, ligaments, tendons, periosteum and subcutaneous tissue throughout the body and giving rise to pain, aching, stiffness and other symptoms.

The lesion consists in inflammatory hyperplasia of the connective tissue in patches of varying size scattered throughout the body.

34 Ray: *Nature, Prevention, and Treatment of Fibrositis*

The new tissue contains fibroblasts and is chronically inflamed with serous or sero-fibrinous exudation in its interstices.

Having regard to this description my subsequent remarks are confined entirely to inflammations of the fibrous tissue associated with the contractile and integumentary systems of the body.

It must be remembered, however, that all joint affections are complicated by changes in their fibrous envelopes, and nodule formations are common, but from a diagnostic and descriptive point of view it seems better not to increase the already chaotic state of our ideas by introducing a term which would lose something of its distinctive character by being so employed. This envelope of fibrous tissue which sends its prolongations everywhere not only forms the muscle sheaths and coverings for tendons and aponeuroses but conveys the blood, lymph and nerve supplies to every part of the body. It must of necessity be intimately concerned with all the biological interchanges of fluids which take place as a result of bodily activity.

As the nature of these changes has an important bearing on what is to follow, it is advisable at this point to call to mind one or two important physiological facts associated with muscular contractility. Du Bois Reymond first showed that muscle is normally alkaline but becomes acid when it works. According to Kite,¹ the protoplasm of the muscle sarcolemma is the most viscous, elastic and cohesive of all living gels. Its particles are arranged in very small units, so that their surface is very large compared with their bulk. Either by the orientation of the molecules of which they are composed, or because they are confined in tubes, they swell in a direction transverse to the long axis of the muscle during contraction.

The effect of a nerve impulse sweeping over a muscle is to cause a combustion of the contained carbohydrates. This produces sarcolactic and other acids. Heat is also liberated. Under the influence of heat and acidity the molecules of the sarcolemma absorb water and swell in the manner just indicated. In a very short time, varying with the length of the contraction, the lactic acid is burned or recombined, carbon dioxide escapes from the muscle and the acidity is reduced. This, in turn, reduces the affinity of the contractile tissues for water which passes out. The elastic properties of the muscle quickly enable it to regain its original shape.

[Reference was made to some experiments in this connexion, viz., those of Dreser and Babinski.]

The change in acidity is to be regarded as intimately associated with the phenomenon of muscular activity. In ordinary conditions of health and in the absence of fatigue there is perfect harmony in the interaction between nervous impulse and muscular response. The mind is only aware of muscular action when there is some obstacle to this smooth response. This obstacle may be considered as due either to the inefficient removal of the products of muscular activity, in other words "clogging," or to changes in the plasma which in some way or other inhibit the proper performance of the metabolic exchange already referred to. This "clogging" appears to take place in the minute lymphatics which run in the fibrous connective tissue.

The occurrence of the thickened indurated areas and of the tender cords or strands which are constantly found among the affected muscles are doubtless caused by lymph stasis, and would account for all the subjective symptoms complained of, viz., stiffness, pain, cramps, tenderness and neuralgia. The same explanation will probably account for nodule formation. The microscopical appearances of the nodules clearly show their inflammatory nature and they must therefore be looked upon as the definite response on the part of the connective tissues to long-continued irritation.

The manifestations just referred to are by no means confined to cases definitely diagnosed as fibrositis. Certain forms of gastric dilatation, especially when associated

¹ Matthews, "Physiological Chemistry," 1921.

with hyperacidity, cause rudimentary forms of tetany with muscular contractions. Dragstedt mentions experiments which show that animals in tetany following parathyroidectomy suffer severe intoxication from the intestinal tract arising from the activities of the proteolytic group of intestinal bacteria, which produces substances for the most part protein-split products of the nature of amines. The production of these protein-split amines or similar substances, their subsequent presence in the connective tissue plasma, and their final inhibition of the metabolic changes already alluded to, appear to have a direct bearing on the causation of fibrositis.

Cold is usually regarded as a frequent cause. The incidence of a stiff neck or an attack of lumbago consequent to sitting in a draught is a very common experience. It has already been shown that heat is a necessary accompaniment of not only muscular action, but of all other activities. In an ordinary healthy individual, cold does not, unless exceptionally severe, produce the symptoms mentioned. The application of cold must therefore only be looked on as the exciting cause. The predisposition is already there,—the match that lights the flare, so to speak.

Although the object of these remarks is to stress what the Chairman has described as the metabolic side of the question, it would be idle to deny that in a great number of instances the removal of obvious foci of infection in cases of fibrositis is quickly followed by marked improvement of the condition. As there is no record of any pathogenic organisms being found either in the nodules or the connective tissues in which they are situated, it would appear more logical to assume that the infective foci, especially when in the mouth, exert their ill effect by causing a condition of chronic ill-health with consequent digestive and metabolic disturbances.

The *prevention* of fibrositis can be summed up as the observation of the ordinary rules of hygiene as regards housing, clothing, food and exercise.

The *general treatment* depends chiefly on the regulation of metabolic errors where possible. Treatment at a suitable spa comes under this heading.

Of the various forms of *local treatment*, such as massage, strapping of affected muscles, application of heat in different ways, &c., by far the most important is skilfully applied massage which has as its object the breaking down of the nodules and the promotion of free circulation in the minute lymphatics.

Dr. C. E. SUNDELL.

In considering the nature of fibrositis one is struck by the multiplicity and diversity of the factors held responsible for its occurrence, and the suggestion arises that these may be merely subsidiary to some deeper and more important influence which prepares the way for their action. May it not be possible that the tissue-soil is more important than the implanted seed?

In this connexion the fate of the chemical products of muscular activity and depression of the eliminative action of the skin have an importance that is apt to be under-assessed. The work of Wilde¹ upon this subject has not yet received from the profession the scrutiny that it deserves but there are signs that his views are meeting with wider acceptance, as clinical experience lends support to his hypotheses.

Certain basal facts which can be confirmed by simple methods of clinical examination appear to provide a clue to the fundamental nature of fibrositis:—

- (1) Sufferers from this condition have a subnormal temperature; the occurrence of transient febrile attacks, associated—as they always are in these patients—with increase of pain, does not contradict the assertion that the usual temperature of the individual is subnormal.

¹ Wilde (Percy), "The Physiology of Gout, Rheumatism and Arthritis," 1921.

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(2) Fibrositis patients have a skin that is naturally inactive or has been allowed to become so. When sweating is induced in these patients the reaction of the sweat as tested by litmus paper is strongly acid; this is in striking contrast to the neutral or faintly alkaline reaction of the sweat of the normal individual.

The acidity of sweat in this condition can be shown to depend upon the presence of large quantities of lactic acid which gives the familiar reaction with Uffelmann's reagent.

(3) Muscular activity, especially in conditions of impoverished blood-supply, is productive of lactic acid which, in the healthy individual, is rapidly excreted in the sweat induced by the exercise. In the case of a sufferer from fibrositis his inactive skin prevents the elimination of the acid, which is therefore held up in the body and enters into chemical combination with the cells. It is noteworthy that fibrositis occurs chiefly in what might be described as backwaters of the circulation, i.e., in structures such as tendons, muscular insertions and fascial sheets.

(4) Under the influence of fever, whether of natural or artificial origin, the combination of lactic acid with the tissues is disturbed and the abnormal chemical substance is set free to circulate in the blood and lymph. So long as the excretory activity of the skin is in abeyance the body is unable to rid itself of the irritant, but if the free outpouring of sweat can be secured the acid load of the tissues is lightened and relief is obtained.

These considerations form the basis for what Wilde has called "pyretic treatment." This consists in exposure of the body to a warm, moist atmosphere for twenty to thirty minutes at a time; visible steam is not used and warmth at a temperature of 105° F. gives the best results.

In institutional work a special thermal couch is most convenient and effective, but it is not portable, and the patient has to be brought to the institution for treatment. Skilled hot-packing affords a trustworthy substitute but is less thorough and rapid in its effects. Recently a portable form of apparatus, suitable for use in the patient's home, has been put upon the market.

During the séance of pyretic treatment the patient's temperature is raised to 100° or 101.6° F. and profuse sweating occurs. Large quantities of acid are excreted and the patient obtains great relief; this relief often precedes a complete cure; all pain and tenderness may disappear although the sweat still remains acid. Unless the treatment is continued until the sweat has become neutral cure cannot be claimed and relapse must be expected.

This line of treatment can, with advantage, be combined with massage and small doses of drugs to relieve acute pain, but it is effectual without such aids and it seems to cut right at the root of the morbid processes upon which the development of fibrositis depends.

DR. HUBERT HIGGINS.

A great number of our colleagues abroad are doing splendid work in applied metabolism, work which I think must prove of the highest value, precisely because it has been done without reference to focal sepsis.

Any view of fibrositis which does not see it as a detail of an integral concept of the general toxic reactions of connective tissue, of Glénard's "Hépatisme" [1] and of subnutrition, is inadequate either for clinical research into its origins or for guidance in treatment or prevention.

Mind apprehends vital phenomena by precisions. I will deal with one of them: the precision of anatomy. About fifteen years ago I took a case of extreme gastroptosis and fibrositis to Vichy to see Glénard. The patient had been told that she could not live more than two years. Glénard's skill in examining an abdomen was like a conjuring trick. Literally, almost as quickly as I speak he had demonstrated certain coarse, unmistakable deviations from the normal anatomical relations. He said: "Your colleagues were right, your patient must inevitably die unless these abnormalities are corrected. They can be corrected. The progress of your case to recovery will be punctuated by their slow return to normal relations." Glénard was an exceedingly successful, busy practitioner. I had gone into his consulting room in

despair, and in less than a quarter of an hour I came out with the certitude of my patient's recovery. Why? Because he had defined a point of departure for therapy in anatomical terms, he had also defined a destination in the same precise terms, and told me how to get there. Without experience in Glénard's methods the effective treatment of a large number of cases of fibrositis is no better than a pious aspiration. For instance, a surgical friend asked me to see a case of intractable pyrexia, with excessive weakness from toxæmia, after an operation. There were generalized hypotonicity, carious teeth, and well-marked fibrositis in the cervical spine. Under treatment with Vichy water, minced meat, fresh potassium salts in vegetable soup and Glauber's salts, the patient, for whom a well-known physician had found no remedy in the morning, recovered the same evening. The teeth were removed during the following week. This is an example of the application of Glénard's doctrines of hepatic insufficiency.

Some years ago Professor Jean Sicard, of Paris [2], asked his colleague, M. Robineau, to remove the perithecal fat of the lumbar spine by laminectomy in six cases of intractable lumbago. This [drawing shown] is the appearance of the perithecal fat in vivisection. The superhydrated tissues bulge. The vertebral canal is not large enough for it. Evidence of this continuous expansive pressure is discovered in the compressed cord and dura mater. I have found that there is a marked scale of variation in the tonicity of the external vertebral connective tissue. This tonicity varies between the watery softness of hypotonicity and the consistency of tough india-rubber. It is common to discover a resistance of over 15 lb. to the square inch, especially on each side of the spinous process. The resistance is most marked over the interlaminar ligaments. When expanding connective tissue is resisted by bone it may partly obstruct large lymphatic trunks, causing inanition and intractable muscular atrophy within their catchment area. This reversible, anatomical complex, with localized obstructive inanition, is best seen in the hand, the obstruction occurring in the carpal space. By using alternate pressure and relaxation (Asiatic massage), from the wrist along the carpal passage to the hand, the obstruction is removed and an opportunity is given of observing the orderly, invariable sequence of the regenerative changes in the tonicity of connective tissue. Two further common examples are found in the pelvis and the spine.

This [figure shown] is an example of lymphatic obstruction of the sacro-sciatic foramen, muscular atrophy and superhydrated, degenerated, connective tissue. Our Parisian colleagues assert that the majority of fashionable women take to bed and suffer tortures during menstruation. French women are amazingly practical and tenacious. After comparing fit and unfit women some of them decided that in the unfit the pelvic musculature was at fault, so they secured the services of an expert in physical training. Here is one of his cases [figure shown]. This Parisian lady is probably now boasting that she can walk twenty miles a day even during menstruation! An abnormal pelvic musculature has been replaced by a set of muscles which all pull their full weight and secure a normal pelvic lymphatic circulation. The atrophic, awkward gait of the majority of women reveals an abnormal, reversible, anatomical complex.

Another common cause of morbid conditions is associated with funiculitis, i.e., fibrositis around the perineural sheath between the dura mater and the nerve plexus. Sicard affirms that there is also an increase of albumin in the cerebro-spinal fluid, indicating venous obstruction. Three cases of fibrositis, the first with neuralgia and migraine, the second with sleeplessness, and the third with chronic acne, had all resisted treatment for more than fifteen years, but were cured as soon as the lymphatic circulation in the cervical spine was restored and the muscular atrophy was corrected.

Without a careful consideration of the "backgrounds" of fibrositis, treatment in a number of cases will be merely palliative, and quacks of all kinds will continue to flourish. An enterprising man who had been a house surgeon in a London hospital

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took a degree in osteopathy in America. He read a paper before a medical society recently, and though he brought only thin, unsubstantial stuff back with him, it is very doubtful whether any one of his critics could have examined a vertebral column even so well as he did.

At least two exigencies emerge from experience in a valid doctrine of aetiology. The first is to assemble and utilize all pertinent and relevant modern foreign methods and the second to scrutinize the state of our art. The second exigency implies a vigorous and rigorous survey of our older precisions and their disciplines. It is unthinkable that the British medical schools will fail to respond to this splendid vision and thus allow its fruits to be gathered by other nations.

REFERENCES.

- [1] GLÉNARD, R., "Hépatisme," "L'Expansion scientifique française," 1922. Roger Glénard reviews his father's work and confirms his conclusions by modern methods of precision. [2] J. A. SICARD, "Les Algies et leur Traitement," in "Questions neurologiques d'Actualité," SICARD and FORESTIER, "Rachalgie lombaire chronique," *Presse Médicale*, January, 1922, No. 5. *Idem*, "Les Lumbago," *Progrès Médicale*, Dec. 14, 1922. [3] GEORGES HEBERT, "L'Éducation physique féminine."

Dr. W. EDGECOMBE (President of the Section of Balneology and Climatology, Chairman),

summarizing the opinions of the various speakers in the discussion said that:—

(1) On the question of a purely metabolic origin of fibrositis as opposed to the infective origin, opinions were divided. It was admitted by all that infection played a predominant part in the aetiology of fibrositis. Some maintained that infection was a factor in all cases, though the site of infection might be difficult to find or might remain undiscovered. Even where an obvious metabolic disturbance was demonstrated the speakers claimed that an infection or subinfection was always present. Others affirmed the existence of a purely chemical or metabolic fibrositis and denied that infection was a necessary factor, basing their views on physiological and biochemical data. Neither position could be regarded as definitely proved. It was thought that further elucidation of the problem would probably proceed on biochemical lines.

(2) Most speakers were in agreement about the commonest sites of infection as stated in the opening address. Others were mentioned as less common, and therefore, likely to be overlooked, such as antral disease and diverticulitis. The consensus of opinion was that almost every kind of pathogenic organism, whether specific or not, was capable of giving rise to fibrositis. The commonest types met with, it was agreed, were the streptococci, and especially the *viridans* group.

No speaker had touched on the possibility of selective affinity.

(3) As to the value of vaccine treatment this was admitted, with certain limitations. Unless the focus of infection could be located and eradicated it was agreed that the vaccine treatment was of little service in effecting a permanent cure. Several speakers had pointed out the need of caution in the use of vaccines, and stressed the necessity for giving small doses, especially in highly sensitized patients. In chronic cases vaccines were considered to be of little use without local measures directed towards improvement of the circulation through the affected parts. (4) As to the measures to be taken to lessen the incidence of fibrositis among industrial workers one speaker, Dr. Glover, had referred to the work that was being done by the Ministry of Health in this department; and had adduced evidence showing that their labours were already bearing fruit in a lessened morbidity from these affections as compared with that in former years. (5) On the value of spa treatment, especially in the chronic manifestations of the disease, there was general agreement.

Though the discussion had brought forth nothing new or startling, the interchange of views and experience served to clarify the subject in the minds of many. The dominant note was the importance of the infective factor in the production of fibrositis.

Sections of Medicine, and Comparative Medicine.

Chairman—Dr. HUGH THURSFIELD (President of the Section of Medicine).

DISCUSSION ON HODGKIN'S DISEASE IN MAN AND ANIMALS.

Sir HUMPHRY ROLLESTON, Bt., K.C.B., M.D.

Synonyms.—Hodgkin's lymphogranuloma, lymphadenoma, lymphogranulomatosis or granulomatosis maligna.

Nomenclature has been a stumbling block, for the terms lymphosarcoma (Virchow) and pseudo-leukæmia have been applied to what we understand by Hodgkin's disease, whereas quite a distinct and different significance now attaches to these two words. Cohnheim in 1865 employed the term pseudo-leukæmia to a condition in which the enlarged lymphatic glands showed the histological structure in leukæmia while the blood did not—in fact to what would now be called aleukæmic leukæmia, the aleukæmic phase of leukæmia, or, probably better, aleukæmic lymphadenosis. Lymphadenoma, which in this country is synonymous with Hodgkin's disease, has the disadvantage that in America and France it is sometimes employed for what would be more accurately described as lymphadenosis, since it does not run the inevitably malignant course. Except for the drawback of the change it might be well to adopt the term, used for seventeen years by Professor H. M. Turnbull and also employed by Ewing, of Hodgkin's lymphogranuloma.

Incidence.—As the nomenclature is a source of confusion, and the clinical diagnosis, especially from lymphosarcoma, difficult, the Registrar-General's returns may not settle whether the disease is becoming commoner, as some have thought, but they show an increase in the last ten years from 280 deaths in 1913, to 371 in 1923.

Criterion of Hodgkin's disease.—As the cause of Hodgkin's lymphogranuloma is unknown, it is necessary to fall back on its histological structure as the only means of defining exactly what is meant by the name; indeed the diagnosis of a given case can be made with certainty only on its microscopic characters; for the clinical features and the response to treatment, especially to radiations, though strongly suggestive, cannot be regarded as final courts of appeal. The histological appearances described independently and almost simultaneously by F. W. Andrewes and Dorothy Reed, in 1902, are so well known that it is unnecessary to do more than mention them, namely (1) diffuse alteration of the structural architecture of the glands as a whole, showing (2) a diminished number of lymphocytes; (3) endothelial hyperplasia; (4) "lymphadenoma cells," and (5) sometimes well-marked eosinophilia. The blood changes are not pathognomonic; there is often a leucopenia, especially in the earlier stages and in the cases of predominant splenic enlargement; when the disease is widespread a polymorphonuclear leucocytosis is common, and in rare instances there is a well-marked eosinophilia, the significance of which is not clear.

Valuable as microscopical examination of an excised gland is, biopsies are not free from fallacies, for although there is lymphadenoma elsewhere, the gland excised may show nothing more than indefinite lymphoid hyperplasia due to simple inflammation or compensatory for the destruction of other lymphatic glands. But Webster

found that biopsies gave more positive results in Hodgkin's disease than in cases ultimately proved to be lymphosarcoma.

Nature.—Lymphadenoma has been thought to be (1) a neoplasm, (2) a transition between a neoplasm and an inflammatory formation, and (3) as seems most probable, an infective granuloma, the responsible virus of which,—in spite of the descriptions of the tubercle bacillus (C. Sternberg; Fraenkel and Much), a Gram-positive pleomorphic diphtheroid bacillus (Bunting and Yates; de Negri¹), and a spirochæte (White and Proescher),—is not yet established. The view that Hodgkin's disease is a neoplasm rests on several points, and perhaps chiefly (1) on the assumption that in its early stage it is confined to existing lymphadenoid tissues, and that, later, it generalizes like sarcoma and invades tissues, such as muscle and bone, which do not contain any lymphoid tissue; this generalization, however, is quite compatible with the characters of the infective granulomas. The second reason is that, in the late stages, the histological characters may become those of a sarcoma, "Hodgkin's sarcoma," as Ewing (1922) calls it. Though if, and how often, this sequence has been actually proved by biopsy and necropsy I do not know; it is said by Ewing to occur often in mediastinal lymphadenoma, but these are just the cases in which a biopsy may be impracticable. Now the various kinds of cells seen in the early stage are much more like the inflammatory changes in the infective granulomas than the structure of a sarcoma, even though a mixed-celled. But Mallory groups together under the term lymphoblastoma, as true tumours, Hodgkin's disease, lymphoid leukæmia, and lymphocytoma. It is a rather different and difficult question whether Hodgkin's lymphogranuloma becomes transformed during its course into Hodgkin's sarcoma, or whether the condition is sarcomatous from the start and becomes more virulent with the progressive impairment of the patient's resistance. On the analogy of chronic irritation as an antecedent of carcinoma and of the rare occurrence of sarcoma and carcinoma in the same growth, it would be reasonable to believe that a gland originally the site of chronic inflammation may later become sarcomatous, and Ewing (1913) has observed this sequence of events in cases in which repeated operations have shown the elimination of the original granulomatous lesion. But it would appear to be an open question whether the sarcomatous change occurs in the cells of Hodgkin's lymphogranuloma or in the tissues around, the latter process being analogous to the occurrence of a squamous-celled carcinoma in the site of cutaneous lupus.

The primary site of lymphadenoma is usually regarded as the cervical glands, as shown by the statement that these are first affected in from 50 (Ziegler) to 76 per cent. (Bunting) of the cases. But it does not follow that the glands first palpably enlarged are necessarily those first attacked; on the rather slender basis of fourteen cases Symmers has insisted that primary enlargement starts in the abdominal or in the abdominal and thoracic glands ten times more often than in the cervical, and Ewing confirms this. Its starting point is of practical importance as determining the extent of the area to be treated by X-rays or radium. A remarkable feature of Hodgkin's disease is that, although its first and main site is in the lymphadenoid tissues of the body, including the spleen, the mesenteric and the retroperitoneal lymphatic glands, it very rarely attacks the lymphoid tissue of the alimentary canal. It is true that cases, such as Pitt's collection of twenty-five cases, have been described, but it is significant how few have been recorded since 1902 when the histological characters were established.

Satisfactory evidence that Hodgkin's disease has ever been transmitted to animals is wanting; Bunting and Yates, after repeated injections of their diphtheroid bacillus isolated from lymphadenomatous glands, obtained appearances in

¹ I am indebted to Dr. James Young for a letter drawing my attention to E. E. A. M. de Negri's later paper (*Folia Microbiologica*, Delft, 1916, iv, pp. 119-187), on the *Corynebacterium granulomatis maligni*, a pleomorphic micro-organism, which appears to be identical with that described by Dr. Young in carcinoma.

five *Macacus rhesus* monkeys resembling "the early changes of Hodgkin's disease as seen in man;" but this is rather ambiguous, for the lymphocytic hyperplasia which Bunting describes in the early stage of Hodgkin's disease resembles inflammation. Other observers have failed to confirm this. Inoculations of material from lymphadenomatous glands into monkeys have given negative results (Longcope; Cunningham and McAlpine; Stewart and Dobson). Stewart and Dobson described "a peculiar giant-celled reaction, probably of foreign body type, around the implanted material," which is of some significance in relation to the early changes of lymphadenoma reported by Bunting and Yates. Twort found that guinea-pigs frequently reacted to inoculation of pieces of lymphadenomatous tissue by the production of transient local nodules which histologically were entirely of an inflammatory nature.

HODGKIN'S DISEASE IN ANIMALS.

The chief interest of to-night's discussion, at which we welcome our colleagues of the Section of Comparative Medicine, is the question of the occurrence in animals of Hodgkin's disease as established by the histological appearances now accepted as characteristic in man. It is described as occurring in the so-called lower animals, but how far is this based on clinical rather than on microscopic evidence either by a biopsy or necropsy? Sir John McFadyean, under the title, "Five Cases of Hodgkin's Disease in the Lower Animals," quotes Sir Frederick Andrewes' account of the histological picture, and adds: "If the characters above mentioned are essential to Hodgkin's disease or lymphadenoma, the cases which I am about to describe have no title to be called by these names."

This frank admission applies to nearly all the few recorded cases of lymphadenoma in animals that I have come across, which might more safely be headed lymphoma; thus in Hodgson's brief account of "Hodgkin's disease in a pig," the glands microscopically "showed simply an excess of lymphocytes above their normal structure." In G. Simons' case of Hodgkin's disease in an Aberdeen terrier there was no post-mortem examination; in Reed's case of Hodgkin's disease in a horse the microscopic appearances of the glands were "a hyperplasia of the cellular elements and an increase in the gland stroma." Hobday's case in a dog, however, was examined after death by Sir John McFadyean, who is quoted as stating that "it was a typical case" without any further details. There does not appear to be any reason why Hodgkin's lymphogranuloma should not occur in animals, but more information is required about the microscopic appearances of cases so diagnosed on clinical grounds.

Diagnosis.

The greatest difficulty in the differential diagnosis of Hodgkin's disease is the clinical differentiation from the variously named primary sarcomas of lymphoid tissue—lymphosarcoma, malignant lymphocytoma, endothelioma. In many cases this can only be made by microscopic examination of an excised gland.

Cases of secondary malignant growth in the cervical and supraclavicular glands may imitate Hodgkin's disease when the primary growth in the mediastinum, or even the oesophagus, is latent and the chest is not skiagraphed. I have seen a case which after imitating Hodgkin's disease became one of *cancer en cuirasse*, so that a small primary carcinoma of the mamma probably escaped detection. I have twice seen the following condition suggest Hodgkin's disease: a primary malignant hypernephroma of the left adrenal or kidney producing a tumour, taken for an enlarged spleen, and secondary glands above the left clavicle.

There are certainly a number of chronic enlargements of a hyperplastic or inflammatory character, though of undetermined origin, which, clinically, are regarded as Hodgkin's disease, and in which the doubt about the diagnosis only arises when

a biopsy or necropsy upsets the clinical opinion. These may be toxic or probably due to a low-grade infection. Ledingham found that the virus of vaccinia, and possibly of small-pox, may set up changes in the cells of the reticulo-endothelial system resulting in an acute granuloma. In chronic *Bacillus coli* infection of the urinary tract I have seen glandular enlargement suggesting Hodgkin's disease. Brill, Baehr, and Rosenthal described splenomegalia lymphatica hyperplastica, a condition showing generalized and gigantic hyperplasia of the lymph follicles of the lymphatic glands and of the Malpighian bodies in the spleen: the blood-count was normal; and the condition was rapidly cured by X-rays; but before this was found out splenectomy was performed in two cases (one followed by death). Cases described as infectious mononucleosis and glandular fever run a short course, and so are not likely to give rise to much difficulty in diagnosis.

There are three clinical forms of *tuberculous adenitis* to be considered in the diagnosis from lymphadenoma; the first is common and often commonplace, the second very rare, and the third so exceptional as to have aroused some scepticism (F. P. Weber; Lyon; Sprunt).

(1) Tuberculous glands in the neck, often clinically simulating early lymphadenoma, especially when the glands show tuberculous large-celled hyperplasia without necrosis or caseation.

(2) Generalized tuberculous adenitis may, as MacNalty showed, be accompanied by the relapsing fever described in lymphadenoma by Murchison (1870), Pel (1885), Ebstein (1887), and often, regardless of strict priority, called the Pel-Ebstein syndrome, for Morgagni in 1652 briefly recorded an example. This generalized tuberculous adenitis, when it occurs, may be associated with visceral infection, for example, of the lungs (MacNalty), though the absence of splenic enlargement, which occurs in about 75 per cent. of generalized lymphadenoma, is of some diagnostic value. In very rare instances, of which Criepe and Narr could not find more than a very few recorded cases, the infection appears to be confined to the glands; in their patient and in another recovery occurred.

(3) The condition, little if at all accepted in this country, described as adenolipomatosis, in which fatty growth occurs around lymphatic glands which may be tuberculous, a process regarded as an effort to localize the disease. In fat persons in the early stage of lymphadenoma the diagnosis from adenolipomatosis has arisen, at any rate in my mind.

REFERENCES.

- ANDREWES, F. W., *Trans. Path. Soc.*, London, 1902, lii, 305. BRILL, N. E., BAHR, G., and ROSENTHAL, N., *Trans. Assoc. Amer. Phys.*, Philadelphia, 1924, xxxix, 371. BUNTING, C. H., "Nelson's Loose-leaf Medicine," iii, 356. BUNTING, C. H., and YATES, J. L., *Journ. Amer. Med. Assoc.*, Chicago, 1913, lxi, 1803; 1914, lxii, 516; 1915, lxiv, 1568. CRIEPE, L. H., and NARR, F. C., *Amer. Journ. Med. Sci.*, Philadelphia, 1925, clxx, 822. CUNNINGHAM, W. F., and MCALPINE, K., *Arch. Int. Med.*, Chicago, 1923, xxxii, 353. EWING, J., *Journ. Med. Res.*, Boston, 1913, xxviii, 1. *Ibid.*, "Neoplastic Diseases," 1922, 2nd ed., p. 373. HORDAY, F., *Veterin Journ.*, London, 1911, lxvii, 486. HODGSON, J. F., *Journ. Comp. Path. and Therap.*, Edin. and Lond., 1903, xvi, 382. LEDINGHAM, J. C. G., *Brit. Journ. Exper. Path.*, Lond., 1924, v, 332. LONGCOPE, W. T., *Bull. Ayer Clin. Lab. Penn. Hosp.*, Philadelphia, 1908, 18. LYON, I. P., *Arch. Int. Med.*, Chicago, 1910, vi, 28. MCFADYEAN, J., *Journ. Comp. Path. and Therap.*, Edinburgh and London, 1903, xvi, 379. MACNALT, A. S., *Quart. Journ. Med.*, Oxford, 1911-12, v, 58. REED, D. M., *Johns Hopkins Hosp. Rep.*, Baltimore, 1902, x, 133. REID, H. A., *Veterin. Journ.*, London, 1922, lxxviii, 202. SIMONS, G., *Ibid.*, 1922, lxxviii, 20. SPRUNT, T. P., "Nelson's Loose-Leaf Medicine," iii, 200. STEWART, M. J., and DOBSON, J. F., *Brit. Journ. Exper. Path.*, London, 1924, v, 65. SYMMERS, D., *Amer. Journ. Med. Sci.*, Philadelphia, 1924, clxvii, 313. TWORT, C. C., *Veterin. Journ.*, London, 1923, lxxix, 21. WEBER, F. P., *Trans. Clin. Soc. London*, 1904, xxxvii, 220. WEBSTER, L. T., *Bull. Johns Hopkins Hosp.*, Baltimore, 1920, xxxi, 458. WHITE and PROESCHER, *New York Med. Journ.*, 1908, lxxxvii, 9. ZIEGLER, K., "Die Hodgkinische Krankheit," 1911, Jena, G. Fischer.

Professor GEORGE H. WOOLDRIDGE.

Hodgkin's disease has from time to time been diagnosed in the so-called lower animals, but it would appear to be very rare in all species except the dog. Unfortunately in the stress of an overcrowded clinical and teaching routine I have not found

it possible to record the cases as they have come under my observation. The various synonyms used leave one in doubt sometimes as to what the true nature of the affection is believed to be, whether a neoplasm, or an infective condition such as an infective granuloma, or a true general lymphadenitis.

In animals, the general characteristic distribution and the histological characters are rather against the suggestion of neoplasm. I am inclined to the view that it is infective, and that it is a lymphadenitis, the causal organism, whatever it is, having a low virulence and producing its effects in the various glands, at first very slowly. The condition in the dog is a symmetrical bilateral enlargement of lymphatic glands with a wide distribution throughout the body and involving the glands in pairs. That it is not due to the tubercle bacillus is shown by the negative reaction to the tuberculin test, the inability to discover the tubercle bacillus before or after death, and the histological characters.

In most of the cases coming under my observation the clinical picture of what I have regarded as Hodgkin's disease has been so characteristic as to leave practically no doubt as to the diagnosis. Unfortunately the condition is often well advanced before one's attention is drawn to it. This is largely due to the insidious nature of the development of the lesions. In those cases, however, that I have seen in the early stages, there has been a slight pharyngitis with a hacking cough and a rise of temperature of 2° or 3° F. The pharyngeal (superior cervical) lymphatic glands are somewhat swollen and tender. A few days later other glands show a similar slight enlargement—notably the pre-scapular, submaxillary, superficial inguinal and the popliteal glands. The appetite is fairly good and often well maintained until the disease is far advanced, but there is loss of weight. This early stage is often unobserved, and in the majority of cases when the patient is first seen the various superficial glands are already considerably enlarged, varying from the size of a walnut to the size of a hen's egg, though the owner has only noticed the "swollen throat." By this time there is a marked loss of energy; the dog will not run about as usual and refuses to go for walks with his master. Any excitement or exertion produces a paroxysm of coughing due to a rapidly-advancing cardiac debility, often with fainting fits. There is now no sign of pharyngitis upon the throat being examined. On palpation of the abdomen the spleen is found to be considerably enlarged, and may be felt extending into the left iliac (or flank) region. The abdominal lymphatic glands appear to be rarely involved. The enlarged superficial glands are firm and have lost the tenderness shown in the early stages. I have noticed in a number of cases that the swelling of the glands subsides and that the consistency softens a day or two before death. The course rarely exceeds two to three months.

I believe that there has been pruritus in some cases in the human subject, and pigmentation of the skin in others, but I have not observed these conditions in animals affected.

With regard to histological examination, all that I can frankly say is that the results are disappointing. The blood shows no appreciable alteration in the number or types of leucocytes present. The spleen, though very considerably enlarged, is normal in consistence and, except for an occasional small lymphoid nodule such as is quite common in the spleen of healthy dogs, it shows no histological abnormality. The enlarged lymphatic glands show only a lymphoid hyperplasia. The histological appearances recorded by F. W. Andrewes and Dorothy Reed, as occurring in the human subject, have not been observed in dogs, and, as suggested by Sir J. McFadyean, if those characters are essential to Hodgkin's disease, it may be that these cases in the dog should not be regarded as true Hodgkin's disease. But one may ask if one can justifiably assume that precisely the same histological picture *must* be present in the same disease in any and every species of animal affected. It may be that such an assumption is begging the question.

I should like to gather some information with regard to treatment, as recoveries

in animals are extremely rare. I have had success only in young dogs up to 12 or 18 months old. In adult dogs it has been invariably fatal, though treatment may prolong the course. Excision of enlarged glands is quite useless, and of course impracticable owing to its wide distribution. The lines I adopt are the avoidance of any excitement or prolonged exertion, and the provision of a highly nutritious and concentrated diet of raw meat, eggs and milk. Medicinally, Donovan's solution (liq. arsenici et hydrargyri iodidi) has given the best results, together with a combination of cod-liver oil, liquid extract of malt, and compound syrup of phosphates; the cardiac debility being controlled by the use of digitalis and squills in alternate weeks. I have no experience of the use of X-rays or radium for this condition, and I have some doubt as to whether the expense of a course of either would be willingly borne by the owner of a dog unless one could give a positive assurance of recovery. I should, however, like to hear what results have been obtained by these means in the human subject.

In the living bovine animal I have met with only one case (in a bull) which I suspected of being Hodgkin's disease. When I saw him in consultation, all his superficial lymphatic glands were considerably enlarged and he had begun to lose flesh considerably. He had given a negative reaction to the tuberculin test. I did not give a favourable prognosis. The treatment I prescribed was Donovan's solution in doses of 1 oz. twice daily, and also cod-liver oil. No blood examination was made. He surprised me, however, by making a complete recovery and was afterwards sold for over £1,000.

I feel I ought not to pass away from this affection of lymphatic glands without reference to a condition in sheep which appears to have no association with Hodgkin's disease, but in which there is a widespread lymphadenitis, often symmetrically bilateral. It may have an added interest in view of the reference of Bunting and Bates to a Gram-positive diphtheroid bacillus as causing lymphadenoma in man. The condition is known as caseous lymphadenitis and is due to a Gram-positive diphtheroid bacillus often called the Preisz-Nocard bacillus. The condition is met with in this country only in the course of meat inspection, and even then may pass unobserved only to be revealed when the roast leg of mutton appears on the table and is cut through at "the Pope's eye," which is, of course, the popliteal lymphatic gland embedded in an island of fat. It has been mainly seen in imported frozen mutton, but recently it has been seen in home-killed sheep. It seems, in these cases, to have given rise to no ill-effects during life, for the body is extremely well-nourished and apparently in prime condition.

The iliac and popliteal glands are the most frequently involved, but cases of much wider distribution are not uncommon. The affected glands become greatly enlarged and caseous, with a tendency to the formation of caseo-pus. I have never seen these lesions in early stages and so cannot say whether there is any resemblance to the glands in Hodgkin's disease. The causal organism, however, is readily demonstrable. The condition is of interest on account of differential diagnosis, and also on account of the widespread lymphadenitis occurring as the result of an infective agent whose channel of invasion is not definitely known, though it may be surmised.

Dr. H. MORLEY FLETCHER.

Within the last two months Sir Humphry Rolleston has given us, in his Schorstein Memorial Lecture,¹ a very comprehensive account of lymphadenoma and of the most recent work done thereon. Having read the lecture and heard Sir Humphry's paper to-night it seems to me that the subject has been dealt with so fully and so admirably that it leaves little for any subsequent speakers to discuss. I shall confine the few remarks I have to make chiefly to certain clinical features of the disease.

¹ *Lancet*, 1925, ii, pp 1209-17.

(1) THE NATURE OF THE DISEASE.

The evidence we have appears to me to point strongly in favour of an infective origin. The so frequent occurrence of a periodic fever of the Pel-Ebstein type is extremely difficult to account for except by the presence of some infective agent, most probably a spirochæte. As will be mentioned later, a periodic rise and fall of this type may be sometimes found even in cases in which the temperature does not exceed the normal. The striking effect of arsenic in the treatment of the disease may be advanced as some support of an infective origin when we compare it with syphilis, rat-bite fever and other spirochætal diseases. The occurrence of an eosinophilia would lend support to this, even though, in my experience, it has been a distinctly rare occurrence.

As regards the relationship, if any, between Hodgkin's disease and malignant disease I have no doubt that occasionally, lymphadenomatous tissues become sarcomatous, and of this I have seen examples; but as to whether the sarcomatous change originates in the affected gland or in the surrounding tissues is still undecided.

(2) CUTANEOUS MANIFESTATIONS.

(a) *Pruritus* may be very severe. It is generally regarded as a fairly common complication though it has rarely been present in cases under my observation. It does not appear to bear any definite relation to the eosinophilia occasionally present in Hodgkin's disease. Arsenical treatment may be the cause of the pruritus, but on the other hand pruritus is sometimes one of the earliest symptoms of the disease and may be present before arsenic has been administered.

(b) *Purpura*.—I have seen extensive purpuric eruptions in cases of undoubted lymphadenoma. It occurs late in the course of the disease and may be of some value in diagnosis. One instance of this was a case of "latent" Hodgkin's disease which closely simulated tuberculous peritonitis, and the appearance of the hæmorrhages led to a correct revision of the diagnosis. In cases which develop purpura it is obvious that leucæmia must be excluded. The purpuric rash may be due to some secondary infection or may be associated with grave anæmia of the secondary type which is so often present in the late stages of the disease.

(3) VARIATIONS OF TEMPERATURE IN LYMPHADENOMA.

(a) *Irregular Pyrexia*.—Most commonly the temperature chart in Hodgkin's disease shows an irregular pyrexia of varying severity. What is the cause of the fever in these cases? It has been suggested by Sir Humphry Rolleston that absorption of the products of necrosis in the affected glands may give rise to the pyrexia. It would be interesting to know whether a relationship between the extent of necrosis and the severity of fever can be established by post-mortem findings.

Again, in this type of case with irregular pyrexia, the possibility of an associated tuberculous infection must be borne in mind, as the fever may be due to, or aggravated by, tuberculosis, which may be regarded as a fairly common complication of Hodgkin's disease.

(b) *Pel-Ebstein Type*.—This form of periodic or relapsing fever is by no means rare, and in fact I believe it to be much more common than was supposed until a few years ago. It is so well known that no account of it is necessary here.

There are two points with regard to this form of pyrexia that I should like to raise. In the first place, what is the general experience as regards the presence or absence of a leucocytosis during the pyrexial periods? I have generally found a moderate polymorphonuclear leucocytosis of ten to fourteen thousand. The second point I wish to bring forward is this: In some cases of lymphadenoma there may be little or no fever—the temperature chart rarely showing a rise

above the normal and then only rising occasionally to 99° F. or 99.5° F. Now in some of these cases if the minimum temperatures are recorded as carefully as the maximum, it may be found that a definite periodicity occurs having the same characteristic rise and fall as the typical Pel-Ebstein curve, but it is revealed below the normal line, not above. A good example of this occurred in a case to the notes of which Sir Charlton Briscoe has very kindly allowed me to refer. This case was a very interesting one of the latent abdominal type of Hodgkin's disease. The Peyer's patches were involved and showed generalized enlargement. They were about three-eighths of an inch thick. Chylous ascites occurred. The temperature chart was practically normal throughout, rarely rising above 99° F. The carefully recorded minimal temperatures, however, showed every seven to ten days a regular rise and fall closely corresponding with the Pel-Ebstein curve with which we are all familiar. I regard it as important that in cases of Hodgkin's disease particular care should be taken to record accurately the minimum temperature as well as the maximum. This remark applies to other diseases, as valuable clinical information may be lost by the omission of this simple precaution—e.g., rheumatic fever in children—the curve may be of pyrexial type, though subnormal. I generally refer to these as a subnormal pyrexia. I suggest that the relapsing type of fever is much more common than it is usually supposed to be, and that it may be present and overlooked in some cases.

(4) CLINICAL TYPES.

(a) The *abdominal* form of the disease in my opinion presents features of greater interest than do either the ordinary external glandular variety or the thoracic type. The abdominal variety is not infrequently of the "latent" type, in that it may show few signs suggestive of lymphadenoma, and may give rise to great difficulty in diagnosis. The external lymph glands may be impalpable and the spleen not enlarged, so that the clinical picture is often indefinite. If the temperature chart shows the relapsing type of fever the problem may be rendered easier of solution.

I may be allowed to quote a case of this kind in a boy aged 8 who was under my care at St. Bartholomew's Hospital. He presented the typical features of tuberculous peritonitis. He was thin and anæmic looking; the abdomen was distended and had the characteristic doughy feel; the spleen was just palpable. There was irregular pyrexia—leucocytes 12,000; occasional diarrhœa. He improved under general treatment during three months' stay in hospital and was then sent to Margate, where he remained about four months. On his return he showed remarkable improvement in every way though the abdomen was still doughy. The temperature was normal. Two months later he was brought up again as he had rapidly become worse—hæmorrhage had appeared on the limbs and trunk, and the spleen was considerably enlarged. He was re-admitted and died shortly afterwards.

Post-mortem, the only enlarged glands present were some in front of the vertebral column and round the head of the pancreas. The enlargement was only moderate. There were lymphoid deposits in the liver and spleen. The glands and spleen showed, microscopically, typical lymphadenoma.

I relate the foregoing case to illustrate the difficulty of diagnosis in the abdominal type, and also as an example of purpura in lymphadenoma.

(b) *Generalized tuberculosis of glands*.—Of this rare form I have seen one typical example. It was one of a group of cases of supposed lymphadenoma under investigation by the late Sir Henry Butlin. All the lymph glands in the body were enlarged and it appeared to be a case of typical lymphadenoma. A biopsy was not made as this was just before the histological features of the disease had been described by Andrewes.

Post-mortem.—The glands throughout the body were softened and caseous.

(5) TREATMENT.

It seems to me that the results of treatment are now definitely better than they were a few years ago. This is doubtless due to advances in X-ray treat-

ment and to the employment of modern arsenical compounds which can be given as intravenous or intramuscular injections. The result of X-ray and arsenical treatment is most striking, though as yet permanent cure has not been attained. The effects of such treatment in the external glandular enlargement, as in the neck, are most marked, and I think in some cases may be permanent, whilst on the other hand the thoracic and abdominal glands, though greatly reduced in size, are very liable to enlarge again in a comparatively short time. I have at the present time under my care a case of Hodgkin's disease which more than a year ago presented great enlargement of the cervical and, to a less degree, of the mediastinal glands. He exhibited a typical Pel-Ebstein temperature curve. Under X-ray and arsenical treatment the cervical glands diminished until they became quite impalpable, and they have remained so for more than twelve months. At the same time the temperature became normal and remained so until a recrudescence occurred a few weeks ago, accompanied by massive enlargement of abdominal glands. I should like to submit this question: *What happens in a group of lymphadenomatous glands under X-ray and arsenical treatment?* Is a favourable result brought about by a destruction of the infection in the area treated, or are the glands so altered or destroyed by the treatment that they are incapable of further reaction?

I should like to conclude my remarks by asking what is the general experience as regards the best form of arsenical compounds in the treatment of Hodgkin's disease, and whether any Fellows have employed antimony compounds, my own limited experience with antimony having given no good results.

MR. LESLIE PUGH.

In discussing the occurrence of Hodgkin's disease in animals, one has to bear in mind two points: first, the fact that it is only one of a group of diseases all of which may show a more or less generalized incidence on the reticulo-endothelial system, and all of which may accordingly be characterized from the clinical point of view by varying degrees of enlargement of the lymph glands, spleen and liver; secondly, a factor that does not arise in human medicine—the economic value of the patient and the idea that it is always possible to make a definite diagnosis by clinical examination alone.

As illustrating these points, one can imagine oneself confronted by an animal showing more or less generalized enlargement of the lymphatic glands combined with the history of a progressive debility. One's diagnosis must in all probability be one of the following: (1) Hodgkin's disease, (2) one of the leukæmias, (3) tuberculosis, or (4) malignant disease. Now whatever one decides to name the disease, the prognosis of a fatal issue is justified and it is quite unusual to suggest the removal of a gland for histological examination before giving one's opinion. On these grounds I must admit that I have no single case that would fulfil the requirements of Andrewes or Dorothy Reed. I have observed animals showing a generalized enlargement of the superficial lymphatic glands—the latter being hard, elastic and discrete—that has first appeared in the cervical region, and there have been no leukæmic changes in the blood; but I have not eliminated the possibility of a leukæmic leukæmia, tuberculosis, or malignant disease for the reasons above mentioned.

I have not seen the so-called Pel-Ebstein syndrome recorded in veterinary literature, nor have I observed anything akin to it. In this connexion, however, it must be remembered that we do not usually have a nurse recording our patient's temperature twice daily, over a period of several months, and therefore it is possible that such a syndrome has passed undetected.

Hutyra and Marek, in discussing the disease, state that Ellermann in his experimental work on transmitting leucosis of fowls, found that a number of his positive cases developed Hodgkin's disease. I have referred to Ellermann's original papers,

and find that the changes he described in the liver, spleen and kidney are true lymphatic hyperplasias and do not fulfil the histological requirements laid down by Andrewes and Reed. The fowl of course has no lymphatic glands. The condition described appears to be a leukæmic leukæmia, as first described by Cohnheim in 1865.

From a clinical point of view all these diseases showing a marked incidence on the reticulo-endothelial system in animals, appear to be the result of an infective process, and I feel justified in making such statements till evidence of the contrary is forthcoming.

Dr. M. J. STEWART.

Two years ago Mr. J. F. Dobson and I published an account of some attempts we had made to reproduce Hodgkin's disease in monkeys by the local implantation of pieces of lymph glands excised from patients suffering with this disease.

Small grafts were introduced into the substance of mesenteric lymph glands in three monkeys (two *Macacus rhesus* and a bonnet monkey), and in two of these an emulsion of Hodgkin's glands was also injected into the substance of the spleen. One *Macacus rhesus*, after four and a half months, showed an unusual degree of simple hyperplasia of the lymphoid follicles throughout the lymph glands generally, and a similar change in the Malpighian bodies of the spleen, the germ centres being specially affected in each instance. Apart from this the only change present was a kind of foreign-body giant cell reaction round the implanted material in one of the glands examined. The other *Macacus rhesus* and the bonnet monkey were under observation for two years and three years respectively before being killed for examination. In neither was there any evidence of pathological or reactive change except that in one of the mesenteric glands there was an abscess containing a nematode.

During the past eighteen months Mr. P. J. Moir and I have made some further attempts to reproduce the disease in monkeys, by the intravenous inoculation of an emulsion of freshly excised glands.

A piece of gland about $\frac{1}{4}$ in. square was cut into small pieces with sterile scissors and ground up in a mortar with 10 c.c. of salt solution. After the grosser particles had been allowed to sediment, 3 or 4 c.c. of the turbid supernatant fluid was taken up with a syringe and slowly injected into the common femoral vein. One bonnet monkey and two *Macacus rhesus* were so treated, but one of the latter died under the anæsthetic. The two which survived were killed and examined after intervals of four and a half months and five months respectively. In the bonnet monkey, the lymph glands showed broadening of the peripheral lymph paths, with endothelial hyperplasia, but no more than was found in the normal controls. The spleen showed nothing of note. In the *rhesus*, one of the mesenteric lymph glands excised for examination contained a small "abscess," in which lay a tiny nematode similar to the one found in Case 2 of the first series. The wall of the "abscess" was lined by a sharply defined palisade-like layer of giant-cells exactly similar to what we had found in the first animal of our earlier series. It is reasonable to suppose, therefore, that on the former occasion also a nematode and not the implanted material may have been responsible for this peculiar cellular reaction. Other glands examined showed considerable endothelial hyperplasia along the lymph tracts, but no more than was present in a groin gland excised from the monkey preceding inoculation.

So far as the production of Hodgkin's disease is concerned, therefore, we have obtained in these five experiments only negative results. Whatever Hodgkin's disease may be at the outset, and in most respects it resembles a granuloma, it is certainly capable of behaving like a neoplasm in its later stages. The development of malignant characteristics, when this occurs, is usually confined to certain regions, even when the original disease has been generalized.

Two recent cases illustrate this point. In the first, a typical case of Hodgkin's disease which had been confirmed by biopsy, the superficial glands, cervical, axillary and inguinal, showed the more chronic fibrous type of change. The lumbar and pelvic glands were of the soft, succulent acute type, and on the brim of the pelvis there was a huge, soft glandular mass

which, microscopically, was indistinguishable from sarcoma. A large malignant ulcer of the stomach, 5 in. by 4 in. in diameter, showed similar histological characters. In the second case, a boy of fourteen, the abdominal lymph glands and spleen presented the typical characters of Hodgkin's disease. In addition, there was a huge malignant-looking mass in the upper part of the right chest, extending through and destroying the chest wall, and filling up the axilla and the root of the neck. There was nodular infiltration and ulceration of the overlying skin. Microscopically, the mass appeared to be sarcomatous.

Professor Dible has to-day shown me the specimens from a case of generalized Hodgkin's disease in which a huge glandular mass in the mediastinum had deeply invaded the root of one lung, with innumerable metastatic deposits, obviously blood borne, throughout the rest of the organ. The microscopic structure, on the other hand, is typically that of Hodgkin's disease, even in the discrete pulmonary deposits. By the naked eye it is indistinguishable from malignant disease.

This malignant change, then, must be regarded as a part of the natural history of the disease, at least in a certain considerable proportion of cases. A parallel may be drawn with granuloma fungoides, in which, however, malignancy seems invariably to occur.

The clinical diagnosis of Hodgkin's disease can only be made with certainty by the microscopic examination of an excised gland, but as Sir Humphry Rolleston has pointed out, even this may be inconclusive. In the early stages of the disease some of the glands, although enlarged, fail to show characteristic changes. Apart from negative findings, which are obviously inconclusive, the chief diagnostic difficulty lies, of course, between Hodgkin's disease and tuberculosis. The form of the latter most likely to cause difficulty is that variety which shows little or no tendency to caseation, and which we are accustomed to describe in our reports as "fleshy." Here, even an opinion based on careful naked-eye examination of the incised gland is almost as likely to be wrong as to be right. In our experience this variety is not infrequently generalized.

In view of this discussion I thought it would be interesting to analyse the results of microscopic examination of superficial lymph glands removed by the surgeon and sent to the laboratory for diagnosis. Such glands, as received by the pathologist, may be classified into three groups:—

- (1) Those which the surgeon believes to be tuberculous.
- (2) Glands from known cases of carcinoma, chiefly of the breast, tongue and lip.
- (3) Glands from cases in which the diagnosis is more or less in doubt.

The first group is usually labelled "Glands, ? tubercle," the second "Glands, ? malignant disease," and the third either "? Hodgkin," "? Hodgkin, ? tubercle," or "? nature."

In Group 1, the provisional diagnosis is almost invariably confirmed on microscopic examination and I have seen only one case in which a gland labelled "? tubercle" proved to be lymphadenomatous histologically. In Group 2, the glands are either cancerous or they are more or less normal. It is the third group which throws light on the difficulties of clinical diagnosis and which I have therefore attempted to analyse with some care.¹ Of glands labelled "? Hodgkin" (forty-seven cases), 25·5 per cent. were lymphadenomatous, 57·5 per cent. tuberculous, 6·4 per cent. lymphosarcomatous and 10·6 per cent. negative or doubtful. Of those labelled "? Hodgkin, ? tubercle" (thirty cases), 17 per cent. were lymphadenomatous, 73 per cent. tuberculous, and 10 per cent. negative or doubtful. Of those labelled "? nature" (383 cases), 4·7 per cent. were lymphadenomatous, 48·5 per cent. tuberculous, 24 per cent. negative or doubtful, 2·4 per cent. lymphosarcomatous, 14·9 per cent. carcinomatous and 5·5 per cent. miscellaneous (mixed salivary gland tumours five cases, simple inflammatory change nine cases, syphilitic adenitis four cases, and inflamed salivary gland, branchial cyst, and multiple neurofibromatosis, one case each).

¹ 460 specimens falling within this group have been examined in the laboratory of the Leeds General Infirmary within the past fifteen years.

The blood changes in lymphadenoma are either so slight or so variable, especially in the earlier stages of the disease, as to be almost valueless in diagnosis. The local eosinophilia so frequently met with in the affected glands, is only occasionally accompanied by a blood eosinophilia. In this, as in so many other conditions, associated with states of slow tissue disintegration (sarcoma and carcinoma, hæmothorax and hæmarthrosis, chronic gastric ulcer, &c.), the eosinophilia is probably due to the presence in the affected tissues of abnormal protein-degradation products, and is without significance in respect of possible protozoal or other parasites.

In view of Dr. Morley Fletcher's remarks, the temperature chart which I exhibit is of interest.

It gives an eighteen months' continuous record of a case of Hodgkin's disease with relapsing pyrexia, and shows how, even in the apyretic periods, there may be an extraordinarily wide daily range of fluctuation. In some of the subnormal periods in the later stages of the disease, the temperature ranges between 93·4 or 93·8 in the morning and 97 or 97·8° F. in the evening for ten days at a time, to be followed by a corresponding fluctuation at a higher level, between 98 and 102, for about a week. Radium treatment was given at intervals for a period of sixteen months, with almost complete disappearance of all superficial glands and with much improvement in the patient's general condition. There was, however, little or no effect on the relapsing pyrexia. The patient died two months after the last treatment, profoundly anæmic and presenting evidences of extensive thoracic and abdominal disease.

Dr. W. H. ANDREWS

said he considered it was important to recognize the exact sense in which the term "Hodgkin's disease" had generally been employed in veterinary literature. In the article by Sir John McFadyean, to which Sir Humphry Rolleston had referred, the names "Hodgkin's disease" and "lymphadenoma" were taken to designate a condition characterized by widespread enlargement of the lymphatic glands, provided that this was not accompanied by any great increase in the leucocytes in the circulating blood, and that no bacteria were found in the enlarged glands.

These names were used in a similar sense by other veterinary writers, but in some of the published reports of cases care had not been taken to render it quite certain that the condition described really conformed to the above definition. In some instances leukæmia had not been excluded by blood examination, and in a number of cases no special precautions were taken to exclude the possibility of the presence of bacteria, and more particularly of the tubercle bacillus. Some authors (as, for example, Sir John McFadyean) had observed all these precautions, however, and a condition answering to the definition undoubtedly occurred in most of the domestic animals, and was not uncommon in the dog.

In this condition, as stated in the passage quoted by Sir Humphry, the histology of the lesions was not similar to that described in human lymphadenoma by Andrewes and Reed. There was a general hyperplasia of the lymphoid tissue, and the connective tissue reticulum tended to disappear or become obscured, so that a section from a diseased gland might show practically no elements other than cells of the lymphocyte type. The disease was described by Hutyrá and Marek under the name of "pseudo-leukæmia," and their account suggested that the lymphoid tissue of the intestine, which was attacked only very rarely in man, was more commonly involved in the domestic animals.

Professor Wooldridge had referred to the caseous lymphadenitis which was induced in sheep by the Preisz-Nocard bacillus; he had mentioned that in England the condition was found chiefly in imported carcasses, and that the sheep appeared not to have suffered in general health. He (the speaker) had seen much of this condition in South Africa, and although it was common to find it post-mortem in sheep which had been killed when apparently in perfect health, yet it sometimes

caused serious illness and death. This was especially the case when extreme enlargement of the bronchial and mediastinal glands caused interference with respiration. The animal then lagged behind the flock, and manifested dyspnoea if driven; the inability to move about and feed properly led to progressive emaciation, and possibly death.

A previous speaker had described the occurrence in human lymphadenoma of the Pel-Ebstein type of fever at a subnormal level. He (Dr. Andrews) had not seen any detailed accounts of the temperatures recorded in the so-called Hodgkin's disease or pseudo-leukæmia of the lower animals; he had, however, seen temperature charts, very similar to those exhibited that evening, in "lamziekte," a bovine disease induced by ingestion of a bacterial toxin.

If the histological changes described by Andrewes and by Reed were regarded as being characteristic of true Hodgkin's disease, and necessarily present in all cases, then, as far as he was aware, no case of the disease had yet been recorded in the domestic animals. It appeared to him that the question of the occurrence of the disease in the lower animals could not be regarded as settled; there was no proof that it did occur in them, but, on the other hand, it was hardly possible to assert with confidence that it did not.

The fact that there was no recorded case which was recognizable histologically as one of Hodgkin's disease, suggested that such cases occurred rarely, if at all. But one had to bear in mind the very considerable differences which might occur in the manifestations of the same disease in animals of different species.

A particular micro-organism might induce, in animals of different species, reactions which varied very considerably in their course, clinical manifestations and anatomical features. In tuberculosis, for example, in the various species of domestic animals one observed differences in the distribution and general appearance of the lesions, and also in the tendency to undergo caseation and calcification, although there were certain general features that were common to all tuberculous lesions. With respect to the influence of species on the general course of a disease, one might recall the fact that a trypanosome infection which in dogs and horses ran an acute course, and caused death within a few weeks, might induce in cattle a chronic infection which was only slowly progressive, and might be of some years' duration.

When considering animals of widely different types, he (the speaker) did not think that one could apply with any confidence a purely histological criterion, however reliable it might prove in connexion with a given species. It seemed to him that the differentiation of the various diseases that might affect the lymphadenoid system, and the comparison of those encountered in different animal species, would continue to occasion much difficulty until we had more knowledge of their ætiology.

Dr. H. H. SCOTT

said that in view of the rarity of the existence, or at least of the recognition of Hodgkin's disease amongst the lower animals, a brief narration of a case which he met with last year at the Prosectorium of the Zoological Society might be of interest:—

The animal, a marmoset—*Callithrix jacchus*—was left at the Gardens on account of a "swelling of the neck." It died a few days later and at the autopsy groups of enlarged glands were found on both sides of the neck, the groins and in the thorax. The thymus was also enlarged and the spleen nearly twice the normal size. The glands on section showed the typical histological changes of lymphadenoma. In addition to the local eosinophilia there was also an increase of these cells relatively in the peripheral blood. The latter was probably accounted for by the presence of *Filaria gracilis*.

It might be suggested that the glandular enlargement was also filarial in origin, analogous to what is found in man infested by *Filaria Bancrofti*. The *Filaria gracilis*, however, lives in the muscle-planes of the shoulder and back, not in the glands; and, moreover, none of the usual changes set up by filariasis were present in the glands, several of which were submitted to microscopic examination.

Dr. M. H. GORDON

said that the discussion had proved most instructive. He was especially interested in the negative result of Professor M. J. Stewart's experiments on monkeys. For some time past he had been impressed by the clinical evidence pointing to a spirochætal agent in this disease. Although he had not worked at the subject recently, he had made a few experimental observations in the past with glands from cases in which lymphadenoma had been diagnosed by microscopic examination.

The animals inoculated with emulsions of these glands were guinea-pigs, and the majority had failed to show any evidence of disease. Occasionally, however, a guinea-pig died after an interval varying from ten days to several weeks, and, post mortem, he could not find any lesion beyond some congestion of the viscera, and no micro-organisms could be demonstrated either by dark-ground illumination or by ordinary methods. As a previous speaker had pointed out, this failure to demonstrate a spirochæte did not necessarily exclude spirochætal infection; but there was no positive evidence, and as some of the control uninoculated guinea-pigs occasionally died in much the same manner, the result of these observations by direct inoculation must be regarded as negative.

The next step was to consult the literature and to find particulars of the methods that had proved successful in the culture of *Spirochæta pallida* under parallel circumstances. An excellent review of these methods by Sobernheim was to be found in Kolle and Wassermann's text-book (Jena, 1913, vol. vii, p. 800). It would seem that the procedure by which the syphilis spirochæte was first successfully cultivated, *in vitro*, was by submerging a piece of syphilitic tissue in a test tube containing a column of serum that had previously been rendered semisolid by heating it to 60° C. After the piece of tissue had been pushed to the bottom of the medium the tube was sealed up and incubated. It was necessary to make a number of such cultures at a time, as only a few were likely to prove successful. In a set of cultures made by this method (of Schereschewsky) from pieces of gland from a case of lymphadenoma and incubated at 25° C., he had noticed in one, after about three weeks, a clearing of the medium around the piece of gland at the foot of the tube. The tube was opened and the contents examined. No organisms were found; so the material was divided into two parts, one of which was heated for half an hour to 55° C. A guinea-pig that received the unheated material died in ten days but showed nothing except congestion of its organs; the other animal remained unaffected.

In the next case he had made use of a modification of the previous method recommended by some Roumanians for the culture of *Spirochæta pallida*. This modification consisted of adding an alkaline solution of pyrogallie acid to the serum before rendering it semisolid by heat—a procedure that made the serum dark brown in colour. Cultures were made by submerging pieces of gland from a typical case of lymphadenoma in this medium and in two out of six cultures made in this way he noticed after three weeks' incubation a bleaching of the medium around the piece of gland. On examining the contents of the first tube he found under the dark-ground illumination microscope what he took to be an actively motile leptospira with twelve to fourteen kinks; but he could only find one, and the companion tube, which was examined later by an expert protozoologist, failed to show evidence of organisms of any kind. These observations, therefore, must also be regarded as negative. Nevertheless, he would strongly recommend those working at lymphadenoma to try anaërobic cultures, and to persevere along the lines that had proved successful in the case of the syphilis spirochæte.

Dr. HUGH THURSFIELD (President)

endeavoured to sum up the discussion remarking that the speakers had cleared the ground to a considerable degree, and had demonstrated that the disease called lymphadenoma in animals was something different from the lymphadenoma of human beings.

**Section of Medicine and Section of Therapeutics
and Pharmacology.**

Chairman—Dr. GEORGE GRAHAM (President of the Section of
Therapeutics and Pharmacology).

**DISCUSSION ON THE TREATMENT OF PULMONARY
TUBERCULOSIS WITH SANOCRYSIN.**

Dr. T. R. ELLIOTT, C.B.E., F.R.S.

SANOCRYSIN and its complementary antituberculin serum have now been used in England by a limited number of observers for a little more than a year. We tried it on human patients because Danish workers had stated that with this drug they could arrest or cure tuberculosis when implanted experimentally in calves. The proof of such laboratory result with animals would compel clinicians to essay every possible means of adapting the treatment to human cases. Møllgaard's experiments on the calf have been criticized, but not, I think, refuted. I hope that we may hear more information this evening on that point, for it lies at the very heart of the whole matter.

Turning, then, to observations on human cases, the first question is that of the movements of the drug through the body. Sanocrysin is a very soluble thiosulphate of sodium and gold, containing 40 per cent. by weight of the latter metal. It is given intravenously as a solution in 10 c.c. of water, and care is needed to prevent the needle from leaving an indelible black spot in the skin. For the first few days after an injection gold can be detected in the urine easily, and to a less amount in the faeces. Frandsen, of Copenhagen, has made numerous observations on human cases and found that only 30 per cent. is so excreted; the rest stayed indefinitely in the body. The only analyses of which I am aware as giving information about the places of storage of that gold were made by Mr. C. R. Harington in two of my cases that died. The tissues were ashed and the metallic gold extracted and weighed.

The first patient died one day and the other twenty-seven days after the last injection. The rapid excretion of gold in the urine is illustrated in the first case, where the contents of the bladder at death, altogether apart from urine previously voided, held nearly 5 per cent. of the gold given. But a large proportion remains stored in the body; Frandsen says, 60 per cent. We recovered only 10 per cent. in the organs analysed—namely, the liver, kidneys, and lungs—but these organs formed only one-twentieth of the body-weight, and therefore the distribution elsewhere, in muscles or in the bones, as with lead, cannot be at a similar concentration. The gold tends to accumulate in the kidneys, as is shown in the second case after twenty-seven days. In this patient it had definitely disappeared from the lungs, which were the only site of tuberculous infection. The drug is therefore not held up for long in tuberculous areas. Its concentration in the kidney was sixty times as great as its concentration in the liver. Even so this patient did not show albuminuria.

We must therefore remember, when attempting to gauge the dosage of sanocrysin, that the concentration in the blood and around the tuberculous areas falls off in a few days, but that a large proportion of the total gold given is stored in the body and that it accumulates, especially in the kidneys.

CLINICAL EFFECTS OF ADMINISTRATION.

The obvious clinical results of administering the drug, in a dose of $\frac{1}{2}$ gr., followed three or four days later by 1 gr., may be briefly recapitulated. There is generally a little nausea, and the patient may vomit once or twice in the first few hours. Some complain of a persistent metallic taste in the mouth with dislike for food. There may be a slight headache. That is all, except in patients with active and well-vascularized tuberculous infections. In these the temperature rises; there is often an intense and widespread rash, scarlatiniform or morbilliform; there may be albuminuria with renal casts, but never any cedema or serious diminution of urine. The general reaction is not one of severe discomfort. But if the drug is pushed unduly there may suddenly develop alarming features, either of hyperpyrexia or of so-called "shock" with fall of temperature, a rapid and weak pulse, hurried breathing, and general collapse. Also, excessive dosage may lead to intense albuminuria, to persistent vomiting or diarrhoea, with complete distaste for food and rapid loss of weight. Most of these features were ascribed by the Danish physicians to the liberation of tubercle toxins from bacilli killed by the sanocrysin, and to combat them a special antituberculin serum was prepared. The features of the reaction as regards the rash, though not the albuminuria, do closely resemble those that were seen with large doses of tuberculin when that method of treatment was first introduced.

But whichever be the cause, whether the tubercle toxins or the ill-effects on the tissues of an excessive concentration of the gold salt, there is very real danger in an ill-regulated use of sanocrysin. There may be sudden or progressive exaggeration of the more serious symptoms of the tuberculous infection, or there may be poisoning of the kidney, of the liver, and even of the skin, with a drug dermatitis that is quite distinct from the relatively transient rash. All these dangerous features are far more liable to arise in the sanocrysin treatment of tuberculous patients than in the use of salvarsan for syphilitic or other infections.

RESULTS OF TREATMENT.

I have treated only eleven cases. Four of these may be discarded, three being of glandular or bony infection and giving no special information, while the fourth was a patient in whom no diagnosis was ever made. That leaves only seven, and two of these died. This number is far too small to justify any sound conclusions being drawn and I can only submit the results of my own experience in the form of impressions.

In the first place, I think that the treatment has not done harm to any case under my care. This statement requires some amplification. There were two deaths during treatment of patients from whom the tissue analyses were made. The first was a hopeless case of tuberculous meningitis; the second was a patient with rapid and very extensive caseation—a "galloping" consumption of the lungs. Here one can only urge a personal judgment, that the patient was desperately ill before treatment was commenced, that he survived a month after the cessation of treatment, and that his downward progress did not seem to have been much influenced for the worse by the sanocrysin treatment.

There was a third case in which for many months I thought that harm had resulted. This was the first case treated in England. At that time the principle which we in London had received from the Danish work as a guide in our trials of the drug was that sanocrysin is bactericidal, but that the tubercle bacilli may soon become resistant to the drug. Therefore it was necessary to push the sanocrysin heavily at the outset and fight at once for victory, even at the cost of some distress to the patient. Grave reactions were to be countered by the use of the special antituberculin serum. It is likely that the acceptance of this principle led to some of the difficulties or disasters that at first were encountered in treatment.

Latterly it has been the custom in Denmark and elsewhere to give smaller doses at longer intervals. Serum is then rarely needed, for the patient is not made ill by the reactions. Of course, it may be that this gentler procedure¹ is not the best way of advancing the cure, but at present one can only judge the problem clinically, for there are no tests available on the pathological side, by examination of the blood-serum or otherwise, which can serve to inform clinicians about the reactions which occur.

To return to the particular patient. She was a girl of 18, of very poor physique and with bilateral apical tuberculosis. During three months she remained in hospital under good routine treatment, yet with tubercle bacilli always present and no improvement. She was then treated heavily with 6 gr. of sanocrysin and with serum, for she had two dangerous collapse reactions. Subsequently she had incessant vomiting for a week, then anorexia and loss of weight. There was albuminuria to 1.5 per cent. On discharge from hospital she was still thin and ill, but she refused to go to a sanatorium and remained at home in a quite poor environment. But she improved steadily. She has now, a year after her treatment, put on a stone in weight. She is plump and well with neither cough nor bacilli in the sputum, and the pulmonary disease is completely arrested. Her urine is normal. My earlier impression was therefore mistaken and in her case the drug not only did no serious harm, but seems to have done good, for her prognosis was originally a poor one. In all subsequent cases I have used less intensive treatment, have rarely employed serum, and have seen no suggestion of harm as the result of giving sanocrysin, but, on the contrary, the treatment has seemed to coincide with a real improvement in each patient.

Is this a Specific Action?

Secondly, the sanocrysin appeared to exercise a specific action on tissues infected by tuberculosis. This was suggested by an unusually inflammatory vascularization of the tuberculous areas in my two cases which were examined post mortem. In other pulmonary cases which did not die there was evidence of a focal reaction in some pain in the chest, slight dyspnea, and often an increase for a while of adventitious auscultatory sounds. There was no proof of the tubercle bacilli being killed directly by the gold salt; but the inflammatory reaction in the tuberculous areas was attended by the escape into the circulation of toxins which produced general bodily reactions similar to those caused by large injections of tuberculin. Such general reactions were seen only in patients with active and well-vascularized tuberculous lesions. But the converse deduction—namely, that a well-marked reaction to sanocrysin is proof of an active tuberculous infection—cannot yet be made, for, so far as I am aware, no clinician has tested the drug in a sufficient variety of other diseases. I tried sanocrysin in one case of tuberculosis of the cervical glands, and in another of a tuberculous fistula from the shoulder-joint. There was no reaction at all and no benefit. The drug was not injected into the fistulous tract itself.

A satisfactory type of reaction occurred in a patient 18 years old, who had an acute and extensive infection of the left lung and less than two months' history of illness. On account of the apparently rapid spread of infection he was kept under preliminary observation in hospital for only ten days. An injection of 1 gr. after a preliminary $\frac{1}{2}$ gr., caused a prolonged rise of temperature accompanied by a generalized rash. The rash recurred briefly with the next injection. There was no albuminuria and no uncomfortable malaise. In all the patient received $4\frac{1}{2}$ gr. in two

¹Fournier and P. Mollaret (*C. R. Acad. des Sciences*, December 7, 1925, vol. clxxxi, p. 943), have, at Levaditi's suggestion, used a gold salt apparently identical with sanocrysin in eighteen cases of human syphilis. Healing and inversion of the Wassermann reaction resulted with repeated doses of 1 gr., but these large doses produced serious general reactions in the patient; smaller doses of $\frac{1}{2}$ to $\frac{1}{4}$ grm. produced very little general effect but they did not control the lesions and they failed to affect the Wassermann reaction.

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months. His general condition improved rapidly after the third injection, his fever ceased, and the tubercle bacilli tended to disappear, while the cough and sputum became trifling. He went home, and two months later had gained 9 lb. in weight, while feeling active and taking long walks. Subsequently he was admitted to a sanatorium from which satisfactory reports of his progress have recently been received. I think that this case was an example of an exceptionally rapid abatement of what appeared to be a serious tuberculous infection.

My impression has been that the best results are seen in patients who react at first with sharp fever and rash. The next injection must then be delayed for a week after the fever reaction, or even much longer, so as to ensure that the following reaction shall be of a less severe character. If the injections are spaced widely enough, dangerous reactions and loss of weight can be avoided and there will never be more than a trifling albuminuria. The albuminuria is certainly related more to the total quantity of sanocrysin given and to the time intervals between doses, than it is to the severity of the reactions in fever and in rash.

Lastly, I wish to refer briefly to two cases of which some account has already been published. One was that of a girl, aged 20, with a localized collection of fluid in the lower abdomen reaching nearly to the umbilicus. The diagnosis of tuberculous peritonitis was not proved by opening the abdomen, but there was a history of pleurisy six years before, leaving persistent physical signs and changes in the X-ray appearance of the chest, and also of tuberculous peritonitis three years before. The patient was treated in hospital for three months without improvement. She was then given sanocrysin, $4\frac{1}{2}$ gr. in seventeen days. She reacted with fever and a rash. At the end of the treatment the fluid had completely disappeared. Five months later there was nothing abnormal to be found on pelvic examination; she had put on more than a stone in weight and she has now returned to work. The diagnosis was reasonably certain and the striking feature of the case was the extremely rapid disappearance, in three weeks, of all physical signs in the abdomen simultaneously with sanocrysin treatment.

The other case was one of equally rapid improvement under sanocrysin, but in which the diagnosis of tuberculous infection was not firmly based. A boy aged 14 developed tuberculous glands in the neck. These were excised and the infection in them proved. He had also had enlargement of the hilum-glands in the chest. After the operation on the neck he developed signs of pulmonary infection. This continued and ultimately the X-rays showed a persistent area of consolidation in the right lower lobe. But there was no sputum and there were no tubercle bacilli in the stools. The boy was under observation for four months in hospital, during which time fever persisted, and there was progressive loss of weight. When treatment with sanocrysin was commenced at the end of this time he was critically ill. He received $1\frac{1}{2}$ gr. in six days. There was a sharp pyrexial reaction and a rash. Soon after this his fever abated and finally ceased. He rapidly regained weight, ultimately putting on 2 st. The signs in the chest slowly lessened and three months after treatment the radiogram of the lung was almost normal.

The clinical history and, though this is rather begging the question, the reaction with fever and rash to sanocrysin, do suggest that the acute pulmonary infection was due to tubercle. In any case the treatment coincided with an extraordinarily rapid recovery in a patient who up till then had been gravely ill—so no harm was done.

CONCLUSIONS.

As I emphasized at the outset, the number of patients whom I have treated with sanocrysin is very small. They were selected as examples in whom any quick improvement of their diseased state would not have been expected under the ordinary routine of treatment. The prognosis of a tuberculous infection is hazardous, even for physicians with long and special clinical experience; and that I do not possess.

But in the cases that I have quoted the turn for the better occurred almost simultaneously with the treatment by sanocrysin; and though coincidences do occur in a most misleading fashion in practical medicine it seems to me unlikely that all these four should have been only chance coincidences. My own opinion is in full accord with that of Professor Faber, of Copenhagen, a physician of very wide clinical experience, who began the use of sanocrysin with perhaps a prejudice against it, but summed up his results in a statement that in sanocrysin he found a drug that produced more rapid improvement in pulmonary tuberculosis than could be obtained by any other method of treatment that he knew.

Professor LYLE CUMMINS, C.B., C.M.G., M.D.

So far between twenty-five and thirty cases have been, or are being, treated with sanocrysin in Wales, and a considerable amount of investigation on laboratory animals has been carried out. It is just a year since the work was begun, and it is possible, in some of our cases, to speak of the effects of a course of treatment several months after the patient had returned to normal life. It is possible, too, to express some preliminary views as to the types of case in which sanocrysin is likely to do good and of the types in which it is likely to do harm.

My colleague, Dr. Norman Tattersall, will be speaking of his cases at Neath, so I shall confine my remarks to a brief consideration of such of my own cases as have been followed up for several months after treatment or in which the patients have died.

Case I.—M. S., female, aged 20. Had to give up domestic service a year before treatment on account of "bad health." Had a serious hæmorrhage eight months before treatment and has had several since. Admitted to Glan Ely Hospital on December 17, 1924. Cough troublesome. Sputum positive. Pleuritic pains left side. Temperature fairly steady but rises above normal ($98^{\circ}7'$ to 99°) in evening. Disease practically confined to upper third of left lung and not advanced. *Weight on January 20, 1925, was 9 st. 3 lb. 3 oz.* A note on prognosis made before treatment ran: "I regard ultimate prognosis as bad, though the immediate prognosis may perhaps be fairly good."

This girl received five doses of sanocrysin intravenously between January 28, 1925, and February 23, 1925, amounting to 4.5 gm. She had rashes and pyrexial reactions and lost weight during treatment, but had no albuminuria. Cough and sputum disappeared (see Chart I), temperature became regular and weight was rapidly regained after the course of treatment. Left hospital on April 15, 1925, weighing 9 st. 13 lb., looking and feeling well; and went to North Wales Sanatorium.

At sanatorium, her weight rose to 11 st. (see Chart II) she did her "grading" successfully, then foolishly left the sanatorium after six weeks against advice and returned home in June, 1925.

After-history.—She has now been over six months at home doing housework. Seen on January 5, 1926, she looks rosy and well, but admits that, latterly, she has felt tired on exertion and has had occasional morning cough and some pain in left side. There is no sputum; but weight has fallen to 9 st. 8 lb. 8 oz. Physical signs less than formerly—but, in view of lassitude, &c., I have advised a further course of sanocrysin.

Result.—In her case the result has been *very good*. The immediate change, even after only five doses, and the complete absence of sputum or of hæmorrhage during the ensuing year, even while at home and doing housework, are to be noted as remarkable.

Case II.—T. J., male, aged 28. Occupation, tin works, since 14 years old. In full work until August, 1924, when he was obliged to give it up owing to pains in side and back and feeling ill. At that time there was not much cough but a little phlegm at odd times all day. In bed at home for twelve weeks and then admitted to Glan Ely Hospital on January 14, 1925. Highest known weight, 11 st. 7 lb., *in clothes*. On February 1, 1925, 10 st. 9 lb. 13 oz., without clothes. Sputum about 2 oz. per day and full of tubercle bacilli. Some cough at night. Short-winded, feels weak and looks pale and ill though well-nourished. Disease almost confined to the right lung, in which there are the physical signs of a cavity in the upper third; which is confirmed in the X-ray film. Temperature irregular, of low type, passing 99° F. at 6 p.m. several times a week. Between February 4, 1925, and March 16, 1925, had six doses of sanocrysin, amounting to 5.3 gm. Lost weight during treatment, and had rashes and transitory albuminuria.

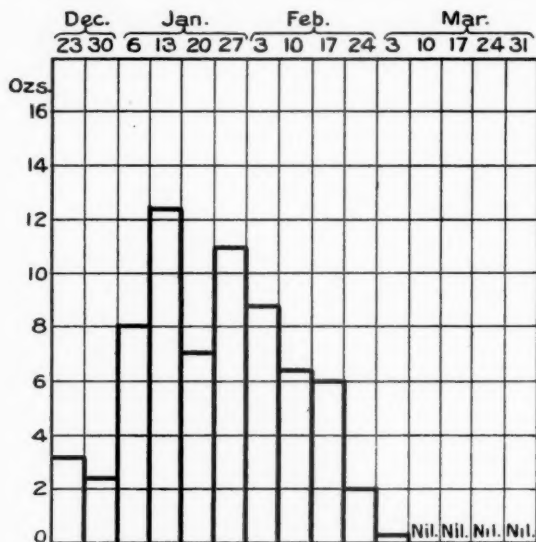


CHART I.
M.S. Chart showing amount of sputum in oz.

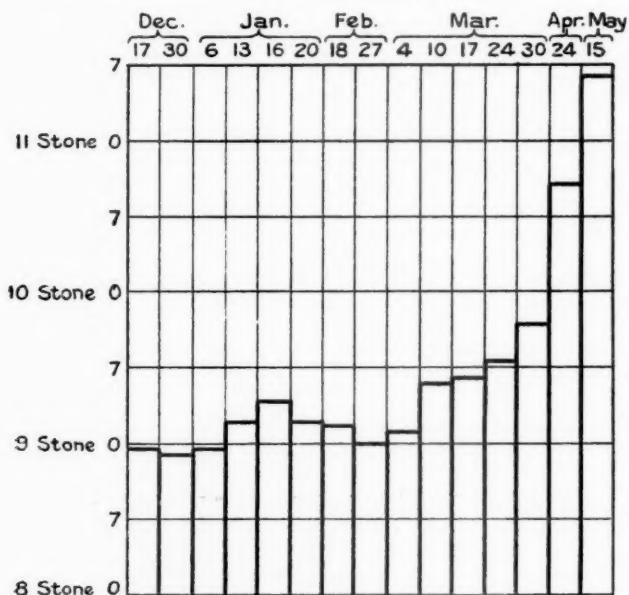


CHART II.
M.S. Weight Chart.

After treatment rapidly regained weight, and was up to 10 st. 9 lb. 4 oz. on April 30, 1925 (see Chart III). Was then sent to the South Wales Sanatorium. Sputum still present, tubercle bacilli very few.

At the sanatorium, did well at first, and sputum became negative. In July, however, he appeared to relapse slightly, and sputum once more became positive. The patient was accordingly given two more doses (0.5 and 1 gm. sanocrysin) in July, the second dose being followed by persistent albuminuria. Since these doses, the patient has steadily gained weight, has reached top grade, and the sputum has continued free from bacilli (see Chart II). He is still at the sanatorium and still has albuminuria.

Case III.—A. J. J., male, aged 15. Collier's assistant. Stopped his work "underground" September, 1924, owing to lassitude and weakness. Referred by panel doctor to the tuberculosis officer, Dr. Melville Hiley. Sputum found positive. Admitted to Glan Ely Hospital in December, 1924. There is considerable disease, chiefly of the "productive" type, in upper half of right lung. The constitutional condition is very good.

Given five doses of sanocrysin, totalling 4.25 gm., between February 25, 1925, and March 30, 1925. Lost weight during treatment, and had rashes and transitory albuminuria.

After treatment rapidly regained weight, sputum disappeared, and, refusing the sanatorium course advised, patient returned to work in a colliery in April, 1925.

Although he felt quite equal to his work, and was actually gaining weight, his sputum returned, and was found to be positive in July. On advice of Dr. Melville Hiley, he returned to Glan Ely on September 29, 1925. Observed for some months, gained weight and lost cough, but sputum was found to be positive, with larger numbers of bacilli than before, on November 2, 1925. A further course of three doses of sanocrysin given between November 9, 1925, and December 2, 1925, totalling 2.25 gm. Since then patient has gained weight, feels well, is doing light work about the hospital, and is now proceeding to the South Wales Sanatorium for a period of graded work and observation.

Case IV.—Mrs. W., aged 24, married. Two children, twins, born 2½ years before treatment started. Patient has never felt strong since the birth of the twins, but the lung trouble was only recognized three or four months ago. Cough troublesome. She is pale, weak, with very little sputum (1 dr. or less per diem), but this is heavily charged with tubercle bacilli.

Admitted to Glan Ely, February 14, 1925. Weight on admission 7 st. 2 lb. 11 oz. Temperature at first fluctuated considerably, even at rest; latterly steadier; but she has had a period of pyrexia with menstruation last week. Was put on "Row's Vaccine," two doses, with slight local and general reaction after each.

Physical Signs.—Dullness, and a few moist crepitations over right lung, upper two-thirds in front, and to just below spinous process of scapula behind. Dullness, bronchial breathing, and crepitations over upper half of left lung behind.

X-ray film shows some loss of translucency at right apex, and a band of pleuro-pulmonary infiltration, corresponding to the line of the second rib in front. There is a glandular mass the size of a pigeon's egg at root of each lung, and a band of pleuro-pulmonary striation on right side, along the level of the sixth rib.

Patient given six injections of sanocrysin between May 22, 1925, and June 29, 1925, amounting to a total of 4.8 gm.

Had albuminuria, vomiting, temperature and a scarlatiniform rash after the second dose (1 gm.). Subsequent doses were well tolerated but patient felt weak and ill, and, after the sixth, declined further doses. A trace of albumin appeared in urine after the last dose and this became marked on July 6, disappearing on July 13, by which date the patient felt much better, was eating well and gaining weight, the sputum now much less in amount. By August 28 she weighed 8 st. 8 lb. 1 oz., felt quite well, had no cough, sputum or temperature; the X-ray film showed improvement and physical signs were less "moist." She declined to go to sanatorium, though urged to do so, and returned to household work at once.

Observed at intervals, she steadily gained in weight and general health, and reported on November 6, 1925, that she felt perfectly well and could do a day's household work and shopping without fatigue. Seen on December 14, 1925, she had caught a cold and was coughing but weight was still increasing. Seen again on January 5, 1926, she had lost 1 lb. 8 oz. in weight, and, though she looked and felt well, and reported cough better and sputum less, and though the physical signs on right side had quite cleared up, a sample of sputum proved to be positive. Have advised a fresh course of treatment.

So much for the favourable cases treated up to June, 1925.

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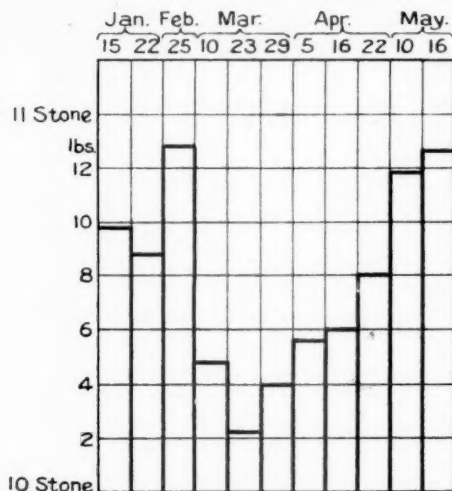


CHART III.
T.J. Weight Chart.

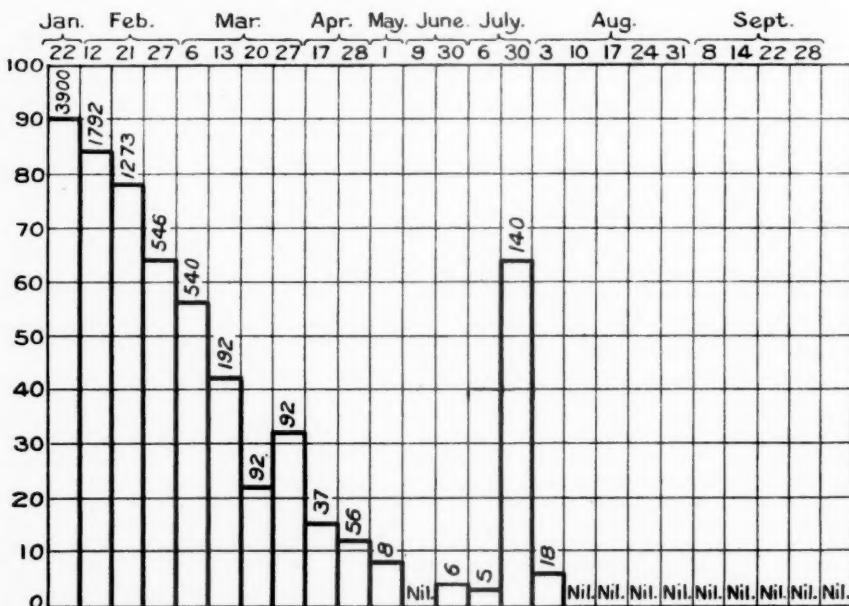


CHART IV.
T. J. Chart showing numbers of fields positive per cent.
[Figures above columns represent number of T.B. in 100 fields.]

Turning now to the unfavourable cases, in spite of the risks known to attend the use of sanocrysin in advanced tuberculosis, I thought it well to give it a cautious trial in the toxic and progressive type of disease so common amongst adolescents and young adults in Wales. For this purpose, I selected two patients in whom the prognosis appeared quite hopeless, short of a therapeutic miracle, and, with the necessary consent, subjected them to treatment.

Case V.—P. D., male, aged 15. Has had cough since October, 1924. Visited the tuberculosis officer (Dr. Gilchrist) in January, 1925. Admitted to Glan Ely Hospital on February 9, 1925. On admission, weight 6 st. 6 lb. 4 oz. (highest known weight, 7 st. 4 oz.). Sputum positive. Temperature swinging to between 99° F. and 100° F. every evening, though at rest.

Physical Signs.—Extensive disease throughout the whole of the left lung as indicated by rales audible everywhere, while there is an area at base of the left lung in axillary line, where the signs suggest definite cavitation. The upper half of the right lung is also compromised. X-ray films show extensive "cotton wool" infiltration of left lung and upper third of right lung.

The patient when first examined by me was toxic and too ill to bear sanocrysin injections though anxious to have them. In the hope of obtaining a temporary improvement, the left lung was partially collapsed, and, after three refills at weekly intervals, he was decidedly better though the temperature was still irregular. A preliminary "diaplyte" course was now attempted, in the hope of raising his resistance, but even 0.1 c.c. of vaccine A led to such a sharp reaction that this course was abandoned and it was decided to try sanocrysin in cautious doses.

Beginning with 0.25 grm. on May 6, 1925, the patient had five injections between that date and June 6, 1925; amounting to a total of 3.35 grm. There were severe pyrexial reactions, some rash and transitory albuminuria, the latter being marked after the final dose of 1 grm. on June 10, 1925.

A disagreeable feature was the appearance of aphthous ulcers on the tongue and cheeks, vomiting and loss of appetite.

This patient appeared to derive no benefit from the injections and to experience much discomfort after them, so the treatment was dropped. The disease took its anticipated course and he died on August 15, 1925.

Case VI.—A. S., female aged 14. A child with a terribly bad family history, both father and mother having recently died of the disease. The patient has been in a home since July, 1924. Right and left upper lobes dull, and crepitations are audible over both. Temperature is of swinging type.

The X-ray film shows extensive mischief at right apex and less extensive trouble at left. The lung-tissue appears to be breaking down at both apices.

This was a typically toxic case and the prognosis, on ordinary treatment, was regarded as hopeless. Three doses of sanocrysin were given, 0.25 grm. on June 8, 1925, 0.4 grm. on June 12, 1925, and 0.5 grm. on June 29, 1925. Each dose was accompanied with a dose of anti-tuberculous serum, to which, however, the patient showed a marked susceptibility. An abscess developed in the left buttock after the last serum injection and it had to be opened and drained. It healed well. As the treatment was clearly of no use, it was discontinued after June 29, 1925. The disease took its anticipated course and the patient died on September 14, 1925.

The only inference to be drawn from these two cases is that sanocrysin is useless at a certain stage in the rapidly progressive toxic type of tuberculosis.

These are the only two unfavourable cases in my own experience so far, but I now have some serious cases under treatment about whom it is too early to speak.

Of the cases treated by my colleagues in Wales, the majority have been dealt with by Dr. Norman Tattersall at Neath, who will be describing them himself.

Dr. Watson has treated four cases at the South Wales Sanatorium. One of these, an old sanatorium patient, in whom treatment was started in July, has had seven doses, amounting to 7.75 grm., which were well tolerated, and the patient, though showing no dramatic improvement, is rather better and his sputum has remained negative since the treatment, having been positive before it.

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In the other three, the courses of injections were only completed in December, so that it is too early to speak of results yet, but Dr. Watson is not impressed so far. In all, the tubercle bacilli have diminished or disappeared from the sputum, and in two the X-ray films suggest improvement. In one case, however, the patient, after seven injections, amounting to 6.25 grm., developed on December 3 a serious skin condition which still persists and now resembles exfoliative dermatitis, causing much discomfort and loss of sleep to the patient.

Frandsen, of Copenhagen, speaks, in a recent paper ("Untersuchungen über Goldausscheidung bei mit Sanocrysin behandelten Patienten mit Lungentuberkulose," *Acta Tuberculosea Scandinavica*, Vol. I, Fasc. 3, 1925, p. 217) of "rare cases of universal dermatitis," so this phenomenon, though regarded as uncommon, appears to have been observed elsewhere. Frandsen thinks it may be due to metallic poisoning and this suggestion has also been made by Dr. Watson about the case in question.

This instance of general dermatitis, and the albuminuria in my Case II (T. J.) which arose after his second course of sanocrysin in July last and still persists, though without any apparent effect upon his health, which is excellent, constitute the only two serious complications which have occurred in cases observed by me; and I think that Dr. Tattersall will have one anomalous result to report.

Frandsen suggests that persistent albuminuria, too, may be a phenomenon of gold poisoning and this opinion is supported by his finding of traces of gold in the urine for as long as a month after a course of treatment. His final conclusion is as follows:—

"It would appear that the albuminuria is the result of the working of the two factors: the harmful effect on the kidney tissue of the tuberculous process on the one hand and of the action of the metal on the other."

That the metallic action suffices, in itself, to produce albuminuria is, however, clear from the experiments on normal dogs carried out by K. Lucille McCluskey and Lillian Eichelberger (*Amer. Rev. of Tub.*, Vol. XII, No. 4, December, 1925, p. 329), who find that "albumin, varying in amounts from a trace to 1.2 grm. per litre, was observed in all cases (of normal dogs dosed with sanocrysin intravenously). The albuminuria increased with increased dosage and lasted for a period from four to ten days with subsequent reappearance." These workers, too, found that gold was to be detected in the urine for considerable periods after the injections, in one case up to the thirty-fifth day. It is clear from these experiments that there is a danger of a "cumulative effect" when using sanocrysin and that the greatest care is necessary in dosage. It suggests itself to me that it may ultimately prove advisable to limit the initial course to five or six injections and to give a subsequent course of three or four more after an interval of two or three months.

It is to be hoped, too, that some simple test for detecting traces of gold in the urine, capable of application as a routine measure in the clinical laboratory, may soon be available, as it is of the greatest importance to be sure that a sufficient percentage of the gold administered is being excreted.

In the meantime, it would seem prudent to avoid giving a further dose until all the effects of the last dose, such as rash, pyrexia, albuminuria, diarrhoea or sore mouth, have quite disappeared. It may prove possible to reduce the dosage below that originally recommended by the Danish workers, but it must be remembered that we are aiming at a definite bactericidal effect and that our efforts are likely to be the more successful the greater the concentration of the bactericidal substance in the blood. By a careful selection of cases and by a prudent *spacing* of the doses, the necessary compromise between efficiency and safety is most likely to be arrived at.

Returning, for a moment, to the four "favourable cases" treated six or more months ago: the most remarkable feature about them is the *dramatic and rapid*

improvement in each of them after a short course of sanocrysin. In three of them the sputum disappeared, and in all of them it became negative for tubercle bacilli. All of them became free from cough, pyrexia if present, and lassitude. All, after a loss of weight during the treatment, got back to, or outstripped, their highest known weight, after the sanocrysin course. On the other hand, in three, after return to work and at intervals varying from four to five months after cessation of treatment, the sputum returned and became positive; while the fourth, though still free from sputum, is showing signs of a return of active disease. It should be added, however, that none of the patients received more than a short course of injections and it is noteworthy that the two who have had a second course of injections appear, so far, to have done well. It can, I think, be claimed that, in these cases, the sanocrysin led to rapid improvement and that this favourable change, though not permanent, was maintained for several months after the course of treatment.

It is claimed by Møllgaard that sanocrysin acts by causing the destruction of tubercle bacilli in the infected body. Let us consider, for a moment, whether our experiences to date throw any light upon this point. The results of periodic sputum examination before, during and after treatment, afford strong support to Møllgaard's claim. In every case so far studied, there has been a diminution in the number of bacilli in the sputum, while, in most of the cases, the bacilli have completely disappeared. In addition, in two cases in which the sputum again became positive some months after treatment, a further course has led in one case to a persistently negative sputum and in the other to a disappearance of all sputum.

My experiments upon rabbits have shown clearly that animals treated with sanocrysin survive for weeks after the death of the untreated controls; also that, in the lungs of the treated animals, when killed for examination, the tuberculous lesions, when present at all, are of a more chronic type and far less extensive than the lesions found in the lungs of the untreated controls.

It cannot be claimed that sanocrysin, in the doses tolerated, is capable of *completely* sterilizing the tuberculous lesions of infected animals or human beings, but it may be regarded as proved that, either by direct bactericidal action or, more likely, through some less direct action in co-operation with the bactericidal powers of the body cells, intravenous injections of sanocrysin lead to a marked limitation of the activity of the tuberculous processes in the lungs and other organs, placing the subject in a much more favourable position for ultimate recovery.

There seems every reason to think that we shall find sanocrysin, judiciously used, a valuable means for raising the less advanced type of "hospital" case up to the "sanatorium" level, and, perhaps, for the actual cure of a proportion of the cases of more favourable clinical type.

DR. N. TATTERSALL.

I have now used sanocrysin in ten cases of pulmonary tuberculosis, in four of which a full course of injections has not yet been completed. The present communication deals mainly with the six cases in which one course of treatment has been completed and only refers briefly to those patients who are still under treatment.

TYPE OF CASE.

So far no attempt has been made to treat the acutely ill, febrile case. The cases under review were all definite cases of pulmonary tuberculosis, with tubercle bacilli in the sputum, and definite physical signs which would bring them into the second or third group of the Turban-Gerhardt classification. They were all more or less afebrile when at rest, but none were so far improved as to be considered suitable for ordinary sanatorium treatment. They were hospital rather than sanatorium cases. Three were of the chronic, proliferative type with evidence of fibrous changes, three were of a more recent and exudative type.

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DOSAGE AND EFFECTS.

Injections were given intravenously at intervals of about a week, an initial dose of 0.5 grm. being followed by four to eight doses of 1.0 grm.

Reactions were frequently severe, especially after the second and third doses. In a typical case the first dose may only cause a small rise of temperature lasting some twenty-four hours. The second dose may lead to a severe reaction with a rise of temperature to 103° F. or more, within twelve hours, gradually falling to normal in three to eight days.

Complications.—Nausea and vomiting have occurred in most cases, coming on within a few hours or even a few minutes of an injection.

Rashes have occurred in six out of nine cases, most often within a few days of the second dose, the whole body being smothered in a morbilliform eruption.

Albuminuria supervened in five out of nine cases, but has never been prolonged more than a week, and appears to be checked if serum is given as soon as it appears.

Abdominal Pain and Diarrhoea occur frequently, and were observed in five out of nine cases.

Loss of Appetite is very marked in the later stages of treatment, but the appetite soon improves when the injections are stopped.

Ulceration of the Mouth occurred in four cases, and in two was very severe, the lips, tongue and buccal mucous membrane being covered with small sloughy ulcers.

Joint Pains were complained of in three out of nine cases but were never severe.

Antitoxic Serum has only been given in those cases in which albuminuria occurred. It was given at once if any considerable quantity of albumin appeared in the urine, and in each case the albumin cleared up very rapidly.

DETAILS OF CASES.

Case I.—E. R., girl, aged 20. History of eighteen months ill-health, with periods of temporary improvement. Physical signs of disease of upper half of left lung, with numerous moist sounds, and recent pleurisy at left base. Slight signs at right apex. Was in hospital for six months before sanocrysin was given, with some general improvement, but there were frequent slight rises of temperature, and sputum remained at 14 to 18 oz. a week, always containing tubercle bacilli. Treated with five doses of sanocrysin in April and May, 1925, reactions moderate, rash and albuminuria. Sputum reduced to *nil* in six weeks, tubercle bacilli greatly reduced in numbers before sputum ceased. Lost 14 lb. in weight during treatment, but regained it and more in two months. Remained free from sputum for six months; since then there has been a slight return, with tubercle bacilli present. Physical signs distinctly improved, and X-rays taken before and after, show very marked clearing, the pleural opacity at the left base having almost disappeared, and the fluffy shadows in the upper half of both lungs being replaced by sharply-defined small reticular shadows, suggesting rapidly progressing fibrous changes.

Case II.—E. H., girl, aged 23. Twelve months history of illness, hæmoptysis, &c. Disease affecting upper two-thirds of both lungs, of recent exudative type. Afebrile on slight exercise. Sputum slight, about 1 oz. per week, tubercle bacilli present. Treated with five doses of sanocrysin in April and May, 1925; albuminuria, rash, and loss of 1 st. in weight. Sputum completely disappeared in a few weeks, and has never recurred in the last eight months. Tubercle bacilli disappeared. Moist sounds in the lungs have mostly cleared up, weight is now higher than ever before, and the X-rays show very marked clearing. The patient has now returned to work.

Case III.—R. W., man, aged 31. History of a weak chest and bronchitic attacks for years, symptoms pointing to tuberculosis of about twelve months duration. Disease of upper third of both lungs with dense consolidation of both apices. Sputum averaged 16 oz. a week, tubercle bacilli present. Temperature frequently 99° F. to 99.4° F. Treated with seven doses of sanocrysin in August and September, 1925. Sputum was reduced in six weeks to 3 to 4 oz. Lost a stone in weight, but has regained it since. Temperature became quite even. Tubercle bacilli were greatly reduced, but have not disappeared. During the last two months the sputum has gradually increased almost to its former amount, and the temperature is becoming less settled. Physical signs have improved, especially as regards moist sounds. X-rays show

marked clearing. This patient is still in hospital, and is to have a further course of treatment.

Case IV.—J. M., man, aged 31. Twelve months history. Disease of the greater part of the right lung, and slight on the left. Sputum 12 oz. a week, tubercle bacilli present. Temperature rather unsteady. Treated with seven doses of sanocrysin, August to October, 1925. Sputum reduced to about half in six weeks. Tubercle bacilli disappeared after fourth dose, and have not been found in seven examinations since. Lost 5 lb. during treatment, regained since. Temperature has become quite normal. Moist sounds have almost entirely cleared up. X-rays do not show any marked change. Patient feels quite well, and has returned to work.

Case V.—L. F., boy, aged 18. Always weak chested, four months history of definite symptoms. Disease of upper half of both lungs of recent exudative type. Sputum 8 to 9 oz. a week, tubercle bacilli present. Frequent rises of temperature to 99°2' F. Treated with six doses of sanocrysin, August to September, 1925. Sputum rapidly decreased, falling to *nil* in fourteen weeks. Tubercle bacilli disappeared after second dose, and were not found in ten subsequent examinations. Gained 2 lb. during treatment, and a further 10 lb. since. Temperature became quite even, and remained so until he had a slight pleurisy, with effusion in December, which is rapidly clearing up. X-rays show very marked clearing, except for the recent pleurisy. This patient is still in hospital.

Case VI.—T. J., male, aged 31. History of over three years of very chronic disease, with several periods of hospital treatment. Signs of extensive disease of the greater part of both lungs, with excavation and fibrosis. Afebrile. Sputum about 16 oz. a week, tubercle bacilli present. Treated with nine doses of sanocrysin, August to September, 1925. Up to the eighth dose there was marked improvement, cough and sputum became much less, and the chest much drier on examination. The ninth dose produced the usual short reaction lasting only twelve hours. Two days later the temperature rose again, and remained irregularly raised for many weeks, swinging from 99° F. to 102° F. There was marked anorexia, diarrhoea, and painful swelling of glands in the neck and iliac fossa. The patient felt very ill, and returned home at the end of October. He remained in bed for another two months, but is now improving, temperature becoming steady, and appetite good. Tubercle bacilli disappeared early in his treatment, and have not yet reappeared in the sputum. I am inclined to regard his severe symptoms, in the main, to be due to metallic poisoning with the gold salt.

The four cases still under treatment are all progressing favourably with similar reduction in sputum and loss of tubercle bacilli from the sputum.

CONCLUSIONS.

From the study of the above cases my general impression is that in sanocrysin we have a substance which produces definite effects on cases of pulmonary tuberculosis, the most marked features being :—

- (1) A rapid fall in the amount of sputum.
- (2) The disappearance of tubercle bacilli from the sputum, at least for considerable periods; when relapses occur it would appear probable that a further course of treatment would lead to further improvement.
- (3) A clearing up of moist sounds in the chest, and X-ray changes which correspond to the clinical findings—both suggesting that areas of disease are undergoing rapid fibrous changes. These changes are much more rapid than are seen in other methods of treatment.
- (4) An improvement more marked in the recent exudative type of disease than in the chronic proliferative type.
- (5) A definite improvement in the temperature chart. Cases which, although not markedly febrile, show frequent rises to 99-99°6' F., with a large daily variation, rapidly develop an even temperature, with a greatly reduced daily swing.

Whether these results are temporary or permanent, only further experience can show, but I feel that the results so far obtained are so striking as to justify further trial.

DR. GEOFFREY MARSHALL

said that he did not think that, at this stage of the discussion, it was possible for Members to appreciate details of further individual cases. He would, therefore, confine himself to a general survey. In June he spent three weeks in Denmark, where he saw nearly 200 cases under treatment, in hospitals in Copenhagen and in sanatoria outside the city, and they bore out, considerably, Professor Elliott's experience in this country. Only one or two physicians there were still using the large initial doses which Secker introduced; smaller doses gave as good results, and there were not the disasters which follow the larger doses in a certain class of cases, namely, those with only a short tuberculous history. Sanocrysin was especially dangerous to those who had had the disease only a short time; the patients did not appear able to resist the reaction, probably because they had not yet had time to produce the antitoxin, if they were tuberculous toxins which were set free by the injection. In Denmark, the serum was being used more and more sparingly, though Secker was still using it in cases in which there were severe reactions. A number of the physicians considered that the serum was antitoxic, or at least did prevent the bad results of too high a dosage. He was shown the records of two patients who had died as the result of the injection of the serum, it being given prophylactically before the first dose of sanocrysin. The symptoms were not the ordinary ones of anaphylaxis. Patients said they dreaded the injections of serum more than they did those of the sanocrysin.

He had himself completed treatment in nine cases only—he only began it last August. He had not used serum, and he had had no alarms. He had avoided giving the treatment in early cases of the disease. In Denmark he saw a patient with a simple tuberculous pleural effusion, in whom the third dose resulted in a very high pyrexia, a toxæmia developed, and the patient had a pyopneumothorax, which he did not think would have happened if he had not received the sanocrysin.

The first of his own cases was that of a child of 16 who had tuberculous pneumonia, and she did very well. At first the sputum was positive, but afterwards was negative, and the signs almost disappeared, the X-ray picture having become practically normal. (He exhibited on the table charts and skiagrams of this case and of the other eight cases.) The next patient had been treated by artificial pneumothorax two years, and then rapidly spreading disease appeared in the other lung. A prolonged course of treatment was given, only with slight improvement. The third case was that of another girl, aged 21, who had what he regarded as a tuberculous broncho-pneumonia, the greater part of one lung showing the typical mottled opacities in the skiagram, but tubercle bacilli were never found in the sputum. She was apparently cured. The next case was that of a man with an eighteen months' history of the disease, with signs of extensive disease in both lungs, and tuberculous laryngitis. The sputum was crowded with tubercle bacilli. He did well, in that his sputum became very much less, and the tuberculous laryngitis completely healed. He still had some bacilli in his sputum, but since going to the sanatorium pyrexia again developed. In some cases the number of tubercle bacilli in the sputum diminished amazingly, from 30 per field to 5 in 150 fields. Another case was not a tuberculous one, but a patient with infective endocarditis, and he treated it as a speculation; there was clubbing of the fingers and enlargement of the spleen, with a temperature ranging from 100° to 104°, and this pyrexia had existed three months before treatment. Small doses caused no effect, therefore large doses were given, and they had an astonishing result on the temperature, which was brought down to normal, and though it did not stay at that longer than a few days after each dose, finally, by giving 2 grm. at a time, it was kept normal eight days. The treatment was not persisted in, as suppression of urine supervened. After a time the pyrexia re-commenced, though not to the same extent as before, and the spleen was no longer palpable. At this stage the patient discharged herself from hospital and went home and I have heard recently that her condition is unaltered.

Dr. F. R. G. HEAF

said he had treated twenty-four cases with sanocrysin at the Warwickshire Sanatorium. Four of these were at stage I, eleven at stage II, nine at stage III. In three of the latter the treatment had to be discontinued because of severe abdominal symptoms. The doses given there differed somewhat from those used by other observers. At his sanatorium a beginning was made with very small doses indeed, i.e., 0.1 gm., increasing rapidly to 0.25, 0.5, then to 0.75, and then 1 gm., the last-named dose being given for a long period at weekly intervals until the sputum became negative. In practically every case the sputum had become negative, and in none of the patients had there been any severe reactions. He had brought for inspection the charts showing a peak temperature which resulted from this method of dosage. In the case demonstrated on the screen, giving the serum enabled a dose of 0.75 of a gram to be reached without any ill-effects, although previously she had been unable to tolerate 0.1 gm. The next temperature chart showed the type of chart which he liked, and which was obtained in practically every case; very little disturbance was caused to the patient, and he got about without difficulty. The next slide represented a case in which he produced artificial pneumothorax on the right side, and the patient became infected on the left side; now, after three months' treatment with sanocrysin, the disease was practically arrested on that side.

He felt that there was a scope for administration of sanocrysin in the cases which had a spread of the infection to the other side. His other cases showed clearing up under sanocrysin.

Sir ALMROTH WRIGHT, F.R.S.

So far everyone who has participated in the discussion has kept out of sight the fact that sanocrysin instead of fulfilling what has been claimed for it has definitely disappointed expectation. Dr. Møllgaard has told us that he was furnishing us with a chemo-therapeutic remedy for tuberculosis—to wit, with an agent which would enter into destructive chemical combination with the tubercle bacillus. That means that it has been claimed for sanocrysin that it will attack and kill the tubercle bacillus in the organism in the same way as the arsenical preparations devised by Ehrlich attack and kill the spirochaetes of syphilis. And, again, in association with this it has been claimed, with respect to toxic effects which supervene upon the administration of sanocrysin, that these are to be referred to, or at any rate should mainly be referred to, poisons, set free from the tubercle bacilli which the drug has destroyed. In other words we are to see in these toxic effects testimony to the tuberculo-bactericidal efficacy of sanocrysin.

Let me point out what consequences might have been expected to follow if that doctrine had been true. First of all, one might have expected all incipient and local tuberculosis—for example, that which we have in tuberculous glands—to have yielded to sanocrysin as rapidly and as completely as the primary lesions of syphilis yield to treatment by salvarsan. Further, it might reasonably have been expected that acute miliary tuberculosis and tuberculous septicæmia generally would have been as tractable to sanocrysin as are the so-called secondary developments of syphilis to salvarsan treatment, and that just as there was no question in syphilis of withholding the remedy because of the intensity of the infection, so also in tuberculosis the most severe cases would be regarded as those which called out most loudly for treatment. And again, just as there is in the treatment of syphilis by salvarsan no risk of lighting up and aggravating the infection by the exhibition of the drug, so also in the treatment of tuberculosis by sanocrysin there should have been no risk of aggravating and lighting up the infection.

The accounts of the clinical results as recorded by Drs. Møllgaard and Secker are utterly at variance with this. It seemed therefore, before everything else, urgent to probe the foundations of Dr. Møllgaard's treatment, and to ascertain whether

sanocrysin, when added directly to the blood and blood fluids, or when administered to patients in the doses prescribed by Dr. Møllgaard and Dr. Secker, did, in point of fact, enter into destructive chemical combination with the tubercle bacillus.

Convenient methods for settling this issue are, in fact, available.¹ Some of those present may remember that I have shown that when tubercle bacilli are implanted into blood or plasma, and when this blood or plasma is introduced into slide-cells and is then incubated for five or more days, the implanted bacilli develop into colonies which are readily visible under the low powers of the microscope and may even be visible to the naked eye. In the plasma clot these colonies can be directly stained by the Ziehl-Nielsen process. In the blood-clot they can be better seen when the hæmoglobin has been first washed out by soaking the clot in water.

Given these methods, it is, as will be realized, a very simple matter, by taking a set of samples of plasma or blood implanted *en masse* with tubercle bacilli, and adding to these samples graduated doses of sanocrysin, to ascertain whether the growth of the tubercle bacillus is arrested or impeded by sanocrysin. And obviously it is an equally simple matter to take a set of samples of plasma or blood from animals or patients before, and also after, the exhibition of sanocrysin, to implant these samples with tubercle bacilli, and to see whether the sanocrysin which has been administered exerts any inhibitory effect upon the growth of the tubercle bacilli.

And the interpretation of such experiments will be quite unambiguous. If a direct addition of sanocrysin to plasma *in vitro* fails to inhibit the growth of the tubercle bacillus we can conclude that the drug as administered does not exert any noxious effect upon the bacillus; and if the plasma of patients and animals taken after the exhibition of sanocrysin furnishes as good a cultivation medium for the tubercle bacillus as plasma taken before the exhibition of the drug, we can conclude that sanocrysin introduced into the blood-stream is not there converted into a tuberculo-bactericidal agent. In the same way when we operate with blood to which sanocrysin has been added *in vitro*, or, as the case may be, *in vivo*, the results will definitely tell us whether the bactericidal powers of the blood as a whole are appreciably increased or diminished by this treatment.

The results of test-experiments made in the manner just indicated will be published in detail by my fellow-worker, Dr. Fry. The results in question show that the tubercle bacillus grows in plasma and blood which have received additions of sanocrysin equivalent to the largest doses which come into application in patients. Moreover, the tubercle bacillus grows in these bloods as luxuriantly as it does in normal plasma and blood. And, more than that, experiment shows that tubercle bacilli will still grow in plasma and blood to which sanocrysin has been added in doses twenty-fold greater than the largest dose employed in the organism. Further test experiments made with the plasma and blood of patients taken after the exhibition of a full dose (1 gm.) of sanocrysin show that the tubercle bacillus grows in such blood and plasma quite as readily as in the samples taken before treatment. The same thing holds true of blood derived from rabbits treated with a quantum of sanocrysin which is the equivalent of 3 gm. of the drug administered to man.

Finally, experiments carried out by my colleague and fellow-worker, Dr. A. Fleming, have shown that even very small additions of sanocrysin to blood notably impair the phagocytic efficiency of the leucocytes.

You will see from these results that the claim that sanocrysin acts as a chemotherapeutic remedy must be absolutely disallowed.

What we are therefore in effect here discussing is whether, when the important claim which was made for sanocrysin has been dismissed, anything else can be said for the treatment. It would seem from the clinical reports that we have heard that

¹ Wright, *Lancet*, February 2, 1924, p. 218.

in certain cases temporary constitutional benefit has been obtained; further, that the sputum, though first increased in quantity, has after a time in many cases been diminished, and that in many cases the sputum for a time becomes free from tubercle bacilli. And we have been shown also, in X-ray projections, that opacities—which are no doubt correlated with patches of consolidation in the lung—have been resolved under sanocrysin treatment. Over against this credit side of the account there is, as you know, though it has not been emphasized to-day, a heavy debit. The patient has to run very serious risks. And perhaps I may add to what has been said about these risks, that in one out of the very few cases of phthisis which I have seen treated by sanocrysin an acute tuberculous septicæmia supervened, a small quantum of the patient's blood obtained at the post-mortem sufficing to convey tuberculous infection to a guinea-pig.

Finally let me add this. Everything that we have here been talking of has, as the Germans in their language pregnantly say, *been there before*. It has all happened before in connexion with Koch's original tuberculin treatment of phthisis. We had there, as I am old enough to remember, the same intense constitutional disturbance with pyrexia. There was reported there also the increase and diminution of sputum, and in many cases also the temporary disappearance of the tubercle bacilli from the sputum. And again we had there resolution and air entry into portions of the lung which before had been quite consolidated (that we may, I think, take as the equivalent of the disappearance of opacities from the X-plates of patients treated by sanocrysin). And to return again to the debit side of the account, there was the frequent lighting up and aggravation of the infection and Virchow's report on the supervention of acute miliary tuberculosis in patients treated with the anti-tuberculous remedy.

On looking back upon these events with such further knowledge as we have now won, there is no longer any mystery in what occurred after Koch's tuberculin inoculations. Koch, by giving inordinate doses of tuberculin, was producing in his patients formidable auto-inoculations. In those who were able to stand up against these auto-inoculations temporary improvement was achieved, with increased air entry into consolidated portions of the lung and also primary increase and then diminution of sputum. In those who could not stand up against the formidable auto-inoculations the negative phase brought aggravation of the infection and in extreme cases acute miliary tuberculosis.

I would suggest to you that what happens in phthical patients treated with sanocrysin is not fundamentally different from that. And let me add that I see in rabbit experiments such as those which were laid before us by Professor Cummins confirmation of this way of thinking. Given a non-virulent infection, such as a human tubercle infection in rabbits, it is not astonishing that an agent which produces auto-inoculations by chemical attack upon the tuberculous foci may, when chance happens to put into the hands of the experimenter the appropriate dosage, exert a favourable effect upon the course of the disease.

Dr. T. R. ELLIOTT (in reply),

said that except for the remarks of Sir Almroth Wright there had been practically no adverse criticism of the method. One was not accustomed to think of Sir Almroth Wright standing as a pillar of any established church, but in this instance he seemed to be insisting on a rigid chemo-therapy, and saying that if a new treatment did not satisfy the requirements of that creed it must be rejected. But he (the speaker) did not feel that such an objection was directly applicable here. The drug might not be immediately bactericidal, even in the body; none the less it might have some therapeutic action, and it did appear to cause a liberation of tubercle toxins.

The essential question was one of simple therapeutics. Was sanocrysin of any use at all, or was it only a golden will-o'-the-wisp that led to no secure ground? Its

first introduction from Denmark was accompanied by strong evidence that it did good in experimentally infected animals, and such laboratory evidence had never been obtained with any other method of treatment. That evidence had not been contradicted, and indeed Professor Cummins' experiments on rabbits tended to support it. The position with regard to sanocrysin was at any rate very different from that which soon developed after the introduction of the other remedy recently suggested for tuberculosis, namely, diaplyte antigen. In that instance, the first broad inquiry initiated by the Medical Research Council revealed no suggestion of benefit; and the animal results were soon found to be invalid. Since the last discussion on sanocrysin in that hall at the meeting of the National Association for the Prevention of Tuberculosis in July, 1925,¹ there had been two steps forward. It had been shown that the drug could be given without serious danger, if proper care were used; and all those who had spoken that evening appeared now to have come to a clear impression that its effect was often beneficial.

Dr. GEORGE GRAHAM (Chairman)

commented on Sir Almroth Wright's description of the tests to which he had subjected sanocrysin. Many substances, e.g., insulin, when tried in a test-tube, had no action, while in the body they were capable of causing profound changes.

¹ *Lancet*, 1925, ii, p. 298.

Section of Dermatology and the Section for the Study of Disease in Children.

Dr. J. H. SEQUEIRA (President of the Section of Dermatology) in the Chair.

DISCUSSION ON THE ÆTIOLOGY AND TREATMENT OF INFANTILE ECZEMA.

Dr. A. M. H. GRAY, C.B.E.

THE term "infantile eczema" is used to denote several different types of superficial catarrh of the skin met with in infants, but I propose to-night to confine my remarks to those varieties which attack the face and which we may appropriately term "facial eczema of infants."

It is not necessary, nor would time permit, for me to enter into elaborate clinical details of these cases. The exhaustive work of Professor A. J. Hall [1] in 1905 has furnished us with a large number of clinical facts, which require no repetition, and I do not desire to tire our colleagues of the Children's Section with other dermatological minutiae which have not much bearing on the main problems of ætiology. It is, however, necessary that I should just refer briefly to the types of facial eczema in so far as they have a bearing on ætiology and treatment.

Various types of facial eczema have been described but I think the majority of cases can be conveniently divided into three types: (1) Those which commence on the cheeks or forehead, which I will call for convenience the primary facial type; (2) those which begin on the scalp, and (3) those which occur in association with a general eczema starting somewhere other than on the face or scalp, for instance in the napkin region.

In the primary face type the trouble usually commences as an itchy patch on one or both cheeks, less commonly on the forehead. The earliest lesions appear to be of an urticarial or erythematous nature and do not to my mind suggest in the least a surface bacterial infection. The rash, when established, varies somewhat in distribution and character in different cases, the prominences of the face suffering more than the hollows, suggesting that friction plays an important part in its production. Itching is intense and spasmodic. Most of the infants are breast-fed, and are fat and healthy looking.

As regards the second type it is very common to find infants with scurfy patches on the scalp, in the early stages in ring-form, later in the form of dark greasy crusts. These patches are often rubbed or scratched by the patient and an inflammatory reaction results. It is not always that the face becomes involved, but when it does there is a tendency for the whole picture of facial eczema to appear suddenly, this suggesting that we are not dealing with a spreading local infection but with a sudden breaking down of skin resistance.

In the third type we have somewhat the same condition, but here the eruption usually begins at a farther distance from the face, and the facial eruption forms part of a general eczemization.

IS THERE A COMMON AETIOLOGICAL FACTOR?

I think it may be useful if the first point we discuss is whether a common underlying factor is present in all these cases, that is to say whether there is a common type of sensitiveness of the skin in all these infants, and whether it only requires some source of irritation to produce an eczematous condition.

It seems to me difficult to come to any definite conclusion by merely studying the dermatological features. The type of the eruption appears to be very similar in all types of case, and whether we find a dry, scaly eruption, or a florid weeping condition, seems to depend more on the state of nutrition of the child and the stage of the disease than on its place of origin. It is a matter of common knowledge that asthma and recurrent bronchitis are apt to occur in children who have previously suffered from facial eczema, but it is not very clear whether this applies to all the types I have mentioned. I thought it might be useful to look into the matter and I therefore wrote to the parents of seventy-five cases that I had seen at Great Ormond Street during the year 1921-22. I received forty replies with the following information: twenty-four of the primary face type, eight of the scalp type, six starting in other regions and two in which the site of origin was not stated. Now of the twenty-four primary face cases ten subsequently developed asthma or recurring bronchitis (nearly half the cases); of the eight scalp cases and six cases in which the eruption started elsewhere, no cases of asthma or recurring bronchitis are reported, while out of two cases the origin of which is unknown one case of asthma occurred.

These figures are to me very striking and suggest that in the primary facial cases we are dealing with some specialized form of hypersensitiveness which is not present in the other types of case. In these latter we may have simply that form of acquired hypersensitiveness which we see in adult types of eczema.

On the other hand the figures are so small that it is impossible to base any definite conclusions on them. They do, however, help to support the view which has been held on clinical grounds that most of the scalp cases were of an infective type, generally referred to as seborrhœic.

I questioned further as to the occurrence of fresh skin eruptions, hoping that I might find some cases of the so-called neurodermatitis or flexural eczema, as this type of eruption is frequently associated with asthma. Five facial cases gave some history of recurrent rash, but all on the cheek. One of the two cases in which there was no history of the site of origin (not the one in which there was asthma) gave a definite history of eczema in the bends of the joints, whilst in none of the cases of types 2 and 3 had there been any further skin trouble. In view of the numerous asthmatic cases, I was rather surprised to find so few cases of flexural eczema, but it may be that some of these will appear later.

If, on the other hand, we look backwards and obtain the past histories of patients suffering from neurodermatitis (or, as I prefer to call it, flexural pruritus), we find a large number of cases which give a history of facial eczema in infancy and also of asthma. It has also been suggested that hay fever and cyclic vomiting occur in the same type of patient and it will be interesting to hear from our colleagues their experiences of this. Even the cases we ourselves see are sufficient, I think, to convince us that we are dealing with some underlying diathesis which does not cease when there is recovery from the facial eczema, but often continues throughout life.

It may be interesting here to mention that five of the forty children had died. One of them (type 3) died when over 4 years old from encephalitis lethargica and need not be considered. The others all died in infancy: one (facial type), from epidemic diarrhœa; one (facial type), from empyema following multiple boils which complicated the eczema. Of the other two, one died of convulsions and the other of some mysterious illness of which I can get no accurate account. In the

latter case the child had recently been an in-patient in the hospital and had been discharged as cured. They both occurred in the scalp type of case. Only in these last two cases is it possible, I think, to consider the question of the so-called "eczema death"; I raise the point, not because these facts help us in the question under discussion, but in the hope that some of our colleagues of the Children's Section may be able to give us some information on this interesting subject.

WHAT BRINGS OUT THE PRIMARY ERUPTION?

In the scalp cases, doubtless, most people will agree that a bacterial infection of the skin is the starting point. It may be a matter for discussion among dermatologists as to what the infecting organisms are, but I will not go into that question now. In cases that arise elsewhere than on the face and scalp, too, some definite cause can usually be found.

In the primary facial cases, however, the cause of the initial lesion is not at all clear. As I have already pointed out, it has not the characters one usually associates with an external irritant, unless it be a factitious urticaria. The two theories to account for the eruption which have attracted most attention during recent years are those of protein sensitiveness on the one hand and digestive disturbances on the other.

It is known that the majority of cases occur in breast-fed children. In Hall's cases (the following figures include all cases of facial eczema) 56 per cent. were fed on breast only, 30.5 per cent. on breast and other food, and 13.5 per cent. on bottle only. F. J. Corper [2] in 100 cases found fifty-seven breast only, twenty-three breast and other food, eleven bottle only and nine of doubtful history, showing an extraordinary similarity to Hall's figures.

Now it follows that if these children are suffering from the effects of specific food proteins the majority must get that protein from the mother's milk, yet the cutaneous tests with mother's milk done by different observers vary to an extraordinary degree. Thus Blackfan [3] obtained positive results in ten cases out of twenty-three, while Corper [2] did not obtain a single positive reaction in 100 cases. At the same time most observers seem to discover an extraordinary tendency in these children to react to proteins, but more often to several proteins than to one. Thus, Schloss [4] out of fifty-three cases tested found that twenty-seven reacted to more than three different foods while thirteen reacted to not more than three. Corper [2] out of 100 cases had thirty-four patients who reacted to more than one protein and nineteen who reacted to one protein only. This tendency to give positive cuti-reactions to proteins is not a feature of facial eczema of infants only, for Blackfan [3] in twenty-seven cases of eczema in patients whose ages varied from 5 weeks to 40 years found twenty-three who reacted to one or more forms of protein.

These results would seem to show that there is no specific hypersensitiveness to food substance in facial eczema of infants, but that these children, like other sufferers from eczema, are prone to give positive cuti-reactions to various proteins.

To return to the question of cuti-reactions to maternal milk, however, I think that such tests would require very careful control. For instance, it does not follow that the substance to which the child is sensitive is present in the mother's milk at the time when the test is done. We must be sure that the mother was ingesting certain substances before testing.

With regard to digestive disturbances, it has long been thought that these constitute a determining factor in the production of facial eczema. The question has been mentioned by most of the older observers, such as Willan and Bateman, Hebra, Erasmus Wilson, Neumann, Besnier and others. More recently careful chemical observations have been made, and some observers fancy that different clinical types of eczema can be associated with indigestion of sugars, starches and fat respectively. After an exhaustive study of the subject Towle and Talbot [5] have come to the following conclusions:—

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"(a) The occurrence of the acute exudative type of eczematous inflammations of the skin is such a frequent association with an indigestion of fats and sugar that it indicates that the process in the skin and the process in the digestive tract probably have some ætiological relationship.

"(b) Contrariwise, the fact noted . . . that the majority of infants presenting the same symptoms of indigestion described above do not likewise present a cutaneous reaction points to the inevitable conclusion that some underlying condition, probably systemic, which the eczematous infants possess, is lacking in the non-eczematous individuals."

This seems to me to be pretty nearly all that there is to be said about the question of digestion and infantile eczema as far as present information goes—though I have noticed in my own cases that a large number show symptoms of overfeeding, such as pumping up of food after the feeds, constipation, and occasionally, though rarely, loose offensive motions; and that they improve remarkably when the quantity of food is reduced. It seems to me possible, or even probable, that indigestion may cause flushing and some itching of the face, and that this may be the reason why the child starts rubbing its face. If the child happens to have the exudative diathesis, or whatever one may prefer to call it, this friction is sufficient to initiate the whole chain of symptoms which are included in the primary face type of the disease. This has been recorded by many observers.

TREATMENT.

Most of us will agree that the main point is to stop friction. This can be accomplished only in a partial degree by methods of restraint. I believe that change of temperature is the most potent cause of itching, and therefore the child should be kept, as far as possible, in a room of equable temperature. An occlusive dressing such as a face mask is also of value in this respect. In non-septic cases zinc paste forms the more suitable basis; in septic cases starch and boric acid or flavine poultices (the latter suggested by Dr. Ferguson Smith) [6]. Itching may further be checked by tar preparations, especially by crude coal tar, in non-septic cases. In fact, there is no remedy which compares with tar in this respect. I am afraid I do not altogether agree with C. J. White [7] that this should never be used on a mask; I generally use 3 per cent. crude coal tar in Lassar's paste on a mask with quite good results, but White's paste is an excellent dressing applied according to his instructions.

I generally find that some reduction in the feeds is all that is required by way of dietetic treatment. As to drugs I rarely use any, and have seen no definite improvement from such drugs as antimony, thyroid, &c., or rarely from intestinal antiseptics. Bromide is occasionally useful.

These remarks, of course, apply to the primary face cases. In the early scalp cases sulphur and salicylic acid ointment are of great value in the early stages, but once the face is extensively involved I think it is better to treat the cases in the way I have described. I do not think we can attribute the facial complications to a mere spread of the bacterial infection, but rather to a hypersensitiveness of the skin, though not of the same character as that met with in the face type, but of the kind seen in adult eczemas.

REFERENCES.

- [1] HALL, A. J., *Brit. Journ. Derm.*, 1905, xvii, pp. 161, 203, 241, 287. [2] CORPER, F. J., *Amer. Journ. Dis. Child.*, 1925, xxix, p. 355. [3] BLACKFAN, K. D., *ibid.*, 1916, xi, p. 441. [4] SCHLOSS, O., *ibid.*, 1920, xix, p. 431. [5] TOWLE and TALBOT, *ibid.*, 1912, iv, p. 219. [6] SMITH, J. F., *Brit. Journ. Derm. and Syph.*, 1922, xxxiv, p. 166. [7] WHITE, C. J., *Arch. Derm. and Syph.*, 1921, iv, p. 793.

Dr. H. C. CAMERON.

No doubt the opportunities for studying this disorder are greater for the dermatologist than for the children's physician. I propose to confine myself to one aspect of the subject and to endeavour to answer the questions: "What is the underlying cause that determines why, of many infants exposed to local irritation, one only develops eczema? What is the nature of this inherited or familial idiosyncrasy? Is there any constant metabolic disturbance of which the eczema is the accompaniment?"

It is not easy to correlate the clinical observations bearing on this question. For instance, how can we explain the regularity with which an attack of measles, for the time being, clears the skin instantly and absolutely of eczema? Again, there is that curious association between vaccination and eczema which has been made use of so much in anti-vaccination propaganda. A small patch of eczema from the moment of vaccination may spread with the greatest rapidity, and this apart from the risk of implanting a generalized vaccinia in the eczematous infant. On the other hand, I have once seen an infant with eczema contract chicken-pox, and the course of the disorder and of the lesions was in every way normal. How, too, are we to account for the tendency towards sudden death? Is the death due to septic infection or to interference with the respiratory function of the skin? Some of the infants who have died suddenly with generalized eczema have had almost the whole surface of the body covered with ointment and confined in bandages. Before death hyperpyrexia has been the rule.

One feature which is peculiarly characteristic of the eczematous infant is the rapidity with which weight is gained and lost. The infants are prone to retain water in their tissues, and often carry a very high content of fluid in their subcutaneous water depots. On the other hand, they tend readily to turn out the water from their bodies so that they become dehydrated with alarming suddenness. When the water has been retained, they commonly exhibit a fixed colour in the cheeks from the eczematous infiltration, they have a large appetite, and their body weight is high. By the public they are generally regarded as peculiarly healthy and sturdy children. Yet, in general, they are fat and flabby with a very poor resistance to all infective disorders. In the dehydrated state, on the other hand, the true condition of atrophy which has been masked by the retention of fluid becomes apparent. It has often been remarked that eczema is especially prone to occur in very thin babies or in very fat babies. Perhaps it would be more true to say that this quality of "hydrolability" or "poikilo-osmosis" is a very constant feature. I show a chart of a baby nine months old now in my ward. At birth its weight was 9 lb. At the end of three weeks it had fallen to 5 lb., and a generalized eczema had appeared. At six months of age, when the weight was 14 lb., fluid was suddenly lost, and in a few days the weight fell to 11 lb. The chart of the daily weighings shows characteristically great fluctuations of body weight. At one time the weight increased by 14 oz. in two days, and a little later there was another sudden rise with a gain of 26 oz. in eight days. It is interesting that both of these sudden increases followed on the removal of milk from the diet and the substitution of a synthetic food, and that both were accompanied by a rapid improvement in the eczema. These huge fluctuations of body weight, these rapid gains and losses, are highly characteristic of the eczematous infant.

The second point to which I may call attention is that this hydrolabile, eczematous infant, whose chart I show, is also spasmophilic, with presumably a low calcium-content in the blood and in the nervous system. For months there has been persistent tetany, and there have been numerous attacks of laryngismus stridulus. It is common to find in practice that eczematous infants show evidence of "manifest" or "latent" spasmophilia. Both disorders, eczema and spasmophilia, are probably associated with a disturbance of balance in the saline constitution of the blood.

The connexion between spasmophilia and eczema is interesting, because there are three conditions in infants in which we find sudden, inexplicable death—eczema, spasmophilia and status lymphaticus. The last of these appears to me to be the post-mortem finding in all children who are in this sense poikilo-osmotic with a high lymph-content in their body. Under such circumstances, provided only that death is sudden and that there has been no dehydration of the body from a long and

wasting illness, status lymphaticus is apt to be disclosed after death. Very frequently in the literature of death from status lymphaticus we find it recorded that the child in infancy suffered from eczema. Some of you may perhaps remember a series of such cases recorded by Dr. Bellamy Gardner before the Section of Anæsthetics and very fully discussed.¹

Between these three conditions—eczema, spasmophilia and the status lymphaticus—which have in common this too great hydrolability, and which are characterized by this tendency to sudden death, there must, I think, exist some relationship. Much of the continental literature is occupied with the discussion of the relationship between infantile eczema and the exudative lymphatic diathesis of Czerny. Czerny's conception of the exudative diathesis covers to some extent the ground occupied by the older description of the status thymo-lymphaticus. A child with the exudative diathesis in general has a high content of lymph in the body; red, rough eczematous cheeks; sparse, irregular hair upon the scalp which has a tendency to wander downwards over the forehead and on to the cheeks. He is apt to be a constant sufferer from impetigo, and has an inveterate tendency to mucous catarrhs of the nasopharynx, bronchi and intestines. After death an overgrowth of lymphatic tissue in all situations is found. During life enlarged tonsils and adenoids are almost always apparent. The enlarged glands are peculiarly apt to become infected with an attenuated form of tubercle. Scrofula may perhaps be defined as that condition in which the tuberculous processes are modified because implanted upon this catarrhal soil. Czerny has written much on the ill-effects of milk for children of the exudative type.

But there is a second group of children in whom the eczema is also common—children with the so-called neuro-arthritic diathesis—meagre, nervous, intellectua children, exhausting their bodies by the energy which they put into all pursuits. Such a child suffers especially from vasomotor disturbances with attacks of pallor, prostration and abdominal discomfort, culminating, in the worst cases, in cyclical vomiting. Such children come most often from a nervous stock with a family history of gout, asthma, eczema and especially migraine. We all recognize the improvement which can be wrought in them by strict limitation of the intake of fat, while at the same time starch, sugar and alkalies are given freely. The child of this type can deal only with small quantities of fat. If more is given acetonaemia ensues, with an increase in pallor, prostration and amyotonia.

It is clear that the tendency to suffer from eczema is at its height during the time that milk is normally the main part of the diet. With the change to a mixed diet, in very many cases permanent recovery occurs. Often the best prescription is to cut short the time of milk feeding, and to give a mixed diet from the sixth month onwards. Even at an earlier age one or two of the milk feeds may be replaced by a similar amount of a vegetable soup.

Finkelstein has attacked the problem from another aspect. His well-known albumin milk was originally designed for the treatment of eczema. Its object is to encourage the dehydration of the too watery infant by a great reduction in the salts and sugars of the food. In the case of the thin, dehydrated infant with eczema other methods must be adopted, but in that of the fat and watery infant albumin milk is capable of giving good results.

On the part played in the production of eczema by hypersensitiveness to specific proteins I am not well qualified to speak, and I should prefer that someone with greater experience should deal with that part of the question.

I believe that too little attention has been paid in this country to dietetic therapy in the treatment of infantile eczema. Eczema is not, of course, produced directly by injudicious feeding, nor does it result from the several types of common gastrointestinal disorder. It occurs only in the predisposed child, and it occurs because

¹ *Proceedings*, 1909-10, iii (Sect. Anæsth.), pp. 19-62.

the reaction of that child to the best possible diet is wrong. Eczema is as common upon breast-feeding as upon bottle-feeding. In breast-fed infants, after the first few months of life, supplementary feeding, or even occasionally complete weaning, may at times bring about improvement.

Dr. H. G. ADAMSON.

The term "eczema" is often employed with so little precision that those who discuss the causes of eczema are sometimes dealing with quite different complaints.

Before we can discuss with advantage the nature and cause of infantile eczema we ought to agree to what form of eruption this term is to be applied. I myself consider that infantile eczema is a very distinct and definite type of eruption. It is a common eruption with features so uniform and so striking that a general description will suffice for each individual case. The eruption starts on the scalp, or on one cheek, and extends until it occupies the scalp, both cheeks and the forehead, avoiding the orbits, the nose and the mouth, thus having a characteristic mask-like distribution. It may be confined to these parts, but usually, sooner or later, it involves the outer surfaces of the forearms and of the legs below the knees, and sometimes, in patches, the trunk.

The eruption consists of circumscribed areas which are red and covered with minute "weeping points." The skin in these parts is swollen throughout its entire thickness, and when pinched up it is felt to be twice or three times as thick as the normal skin. There is intense itching, so that the baby rubs its face against anything with which it can come into contact, or, if old enough, scratches with its fingers or with its toes. When protected from rubbing and scratching, or from other external irritants, the eruption subsides. If scratched or rubbed, or otherwise irritated, it is aggravated. With careful protective treatment it eventually disappears and the patient may never again be affected either in infancy or childhood, or in later life. In cases which are not cured in infancy, however, the eruption, with somewhat altered distribution, may continue into childhood, or even into adult life. Nearly all chronic eczemas of childhood have their beginning as infantile eczemas. In a small percentage of the uncured cases of infantile eczemas asthma develops in childhood, in conjunction with the chronic eczema.

Pathologically, infantile eczema is a catarrhal inflammation of the skin, characterized by serous exudation into the whole thickness of the skin,—a serous exudation which comes to the surface as minute "weeping" points.

As regards the *etiology* of this dermatitis, it may be asked: Is it merely an inflammatory reaction in a skin hypersensitized by external irritants? Or is it a special and peculiar form of dermatitis occurring in certain infants as a manifestation of some abnormal constitutional condition?

My own experience leads me to the conclusion that the type of eruption I have described is at any rate quite independent of any digestive disturbance or of any food idiosyncrasy. I have never been able in any way to influence an infantile eczema by any special form of diet. That external irritants play a very important part in its causation I am firmly convinced. But whether they act merely as excitants of a hypersensitiveness of the skin in otherwise normal children, or whether there is another factor, an abnormal constitutional state which renders an infant particularly sensitive to external irritants, I am in doubt.

I am inclined to think that external irritants constitute the sole factor in the production of infantile eczema. The face—including especially the cheeks and the forehead—is the part most exposed to such irritants as sudden changes of temperature, on imperfect drying in cold weather, or to contact with the perspiring skin of the mother. The baby may be taken from a warm room into the cold air, or from the cold air to the fireside. At first there is merely a flushing or an erythema. Further

irritation leads to a definite dermatitis and finally to an eczema. The skin having become eczematized in one part, becomes hypersensitive in other parts, as we know may happen in adult eczema. From this point the eczema is kept up and aggravated by rubbing and scratching. In one of the soundest contributions to the aetiology of infantile eczema, Dr. Arthur Hall, of Sheffield, has pointed out that in 95 per cent. of his cases the onset was in the winter months, when the exposed skin, (i.e., the face) would be most frequently subjected to sudden temperature changes. In infantile eczemas which start from the scalp, there is always an antecedent "scurfy condition," which is conceivably the source of a local irritation.

One fact only makes me doubtful whether we can ascribe infantile eczema entirely to local causes, and that is the occasional association of infantile eczema with asthma, a circumstance which seems perhaps to suggest an underlying constitutional factor, responsible for both the asthma and the eczema.

In favour of the purely "accidental and external" theory are the facts that eczema may attack only one infant in a family, or even only one of twins, and that infantile eczema may be cured, and indeed, in my experience, can only be cured, by external treatments.

Although I have seen a very large number of babies suffering from infantile eczema, I have not personally met with a case of sudden death, so that I feel that it must be a rare occurrence. Possibly, as Dr. Arthur Whitfield has suggested, the true explanation of the reported cases is that the children have been exposed to chill during the dressing of an extensive eruption, as may also happen in the case of an extensive burn.

Dr. F. LANGMEAD

said that under the name "eczema" appeared to be included many conditions of varied aetiology. If skin diseases were classified in the same way as other diseases in medicine, it would be necessary to take out of the eczema group traumatic lesions of the skin, lesions due to heat or to cold, and conditions due to vascular disturbance, as well as some diseases due to nervous disorder. "Eczema" in his (the speaker's) view, was one of the numerous words in medicine which covered many differing conditions, and such a confusion really interfered with the discovery of causes. If only the profession could get away from the hypnotism of the name, or translate it into the English equivalent "weeping" or something of the kind, it would soon be apparent that there must be some further differentiation in order to secure a movement forward in the understanding of the disease. Some dermatologists appeared to regard eczema as a condition of the skin predisposed by undetermined internal causes, and so separated it from "dermatitis"; others did not make this distinction. If "eczema" were known as an acute, or as a subacute, catarrhal dermatitis a definite disorder would be implied and one which could be studied as a definite entity.

He thought that the type of skin liable to eczema was sometimes inherited, sometimes acquired, and sometimes both inherited and acquired. In considering aetiology, one had also to think of irritants such as soap, soda, wind, heat, scratching, &c., also irritants in the excretions, such as urine and faeces and sweat, and irritants in discharges, possibly also in the blood.

He would consider only three of the varieties of eczema.

(1) He wished first to speak of the eczema which began about the buttocks or in the groins of a small baby, arising as the result of irritation from the urine and faeces. The stools in these cases were often ammoniacal, and the urine was often very acid. He could not think that such cases should be treated only by external measures; the stools and urine should be rendered less irritant. He acknowledged that it was not a purely local condition, because in the same children there were sometimes patches of eczema in other situations—an evidence of the importance of the special susceptibility of the skin. This class of child took carbohydrates badly. Possibly,

even in breast-fed children, it was the carbohydrates in the mother's milk which were concerned in the disturbance. If the faeces were made alkaline by diminishing the carbohydrates, as by putting babies on to whole milk, thereby giving protein in excess, and the urine made less acid by giving alkalies, much could be done towards improving and perhaps curing the dermatitis of the buttocks. Sometimes there occurred an intertrigo which would not heal until attention had been paid to the prepuce: continual dribbling and wetting might occur from a long prepuce, and circumcision should constitute part of the treatment. In carbohydrate dyspepsia the type of child was not far removed from that to which Dr. Cameron had referred, namely, the child whose tissues retain a large amount of water.

(2) The second variety of eczema that he (Dr. Langmead) wished to consider was the facial, in which the condition spread from the face over the body and affected the scalp, and in which the child was apparently extremely well nourished. He believed this type differed from that just mentioned, and considered that there was some predisposing internal condition, at present obscure. It was from this form of disease that occasional sudden death occurred. Dr. Cameron spoke of the sudden death as being associated with status lymphaticus. He (the speaker) was very sceptical about the existence of status lymphaticus in most of the cases in which it had been described. If a child in good nutrition died suddenly, the lymphatic structures and the thymus were found to correspond generally to the status lymphaticus. At one time he had weighed the thymus glands of children who had died suddenly from adequate reasons—being run over by an omnibus or some such cause—and had found the weights to be equal to those generally regarded as excessive in the cases described. Neither had he seen any association between eczema and cyclical vomiting. Patients who suffered from cyclical vomiting did not seem to be particularly liable to eczema.

(3) A third variety of eczema was that ascribable to protein idiopathy. Every one recognized the association between eczema and asthma, itself a symptom-complex of varied aetiology. One of the causes of asthma was protein idiopathy, and there was also a considerable field to be explored with regard to the protein reactions in eczema. Once or twice he (the speaker) had seen children in whom epileptic convulsions were always heralded by the appearance of a patch of eczema. There were relationships between eczema, asthma and epilepsy, which precluded eczema from being considered purely as an external disorder.

The last point was one which he would only mention by way of arousing comment. He was of opinion that much improvement was brought about in intractable cases by giving calcium lactate in sufficient doses. He did not wish to be understood as criticizing the value of local treatment, with which the dermatologists were more competent to deal.

Dr. J. M. H. MacLEOD

said that the modern dermatologist had a definite view as to what might be termed the eczematous reaction, and this was that it did not differ from the various forms of dermatitis produced by irritants which were known. Eczema was not a simple entity like psoriasis, but was a type of reaction. It could be better studied in the infant than in the adult, because in the former there were not the complicating factors which might be present in the adult, such as worry, mental disturbance, &c., and one was reduced to a rather limited aetiological possibility. His (the speaker's) own view on the matter was much the same as that so well expressed by Dr. Adamson. He had had twenty years' experience in a children's hospital in London and had now a wider field of observation in the Metropolitan Asylums Board, and the conclusion at which he had arrived was that the eczematous reaction was a local condition, locally produced by scratching and rubbing. All infants' skins were sensitive, and were made more so by various factors, temperature being one of the

most important. With regard to the internal factor in its causation, it was well known that eczema in infants was much more prevalent in winter than in summer, while gastro-intestinal troubles were commoner in summer. He (the speaker) had never known of an eczematous reaction being produced in a child by a definite error in diet, though an itching of the skin might be produced by something of the kind. Dr. Langmead had spoken of a type of eczema which was located in the napkin area; but eczema was very rare in that situation; what was referred to was either a disease described by Jacquet,—an erythematous condition which was sometimes toxic or was associated with a papular urticaria, or a local streptococcal infection. Irritation he regarded as the main factor in adult eczema also. The moment this reaction was produced, the skin became hypersensitive all over, and when in that state it reacted to all kinds of minor irritants which in normal conditions would have no effect.

With regard to sudden deaths connected with eczema, they must be extraordinarily rare. In all his experience he had known only one such death, the cause of which could not be determined. If eczema were no longer regarded as a specific disease due to an individual cause, like psoriasis, but as a type of reaction caused by some local irritation, generally scratching, our view of it would be simplified, and we could concentrate on the various factors which led to scratching.

Dr. G. H. LANCASHIRE (Manchester)

said that both Dr. Adamson and Dr. MacLeod had expressed his (the speaker's) own view on the aetiology. The bulk of cases of eczema in the infant, excluding those of definitely parasitic origin such as the seborrhœic type, were simply an expression of a skin which was sensitive to external irritation. That was a reasonable conception when one considered the antenatal conditions of the baby's skin, bathed in amniotic fluid. He (Dr. Lancashire) was not prepared to say that cases of eczema were not influenced by metabolic disturbances—in fact he thought they were so influenced—but the great factor was the external irritation. In most cases the condition could be cured by simple local applications. Many of the infants were in perfect general health. In a considerable proportion of the cases of eczema—not only hospital cases but also private ones—the skin was in a state of great neglect with regard to impetigo and other septic conditions, and thus they were first in need of cleansing.

It was now many years since his (the speaker's) attention was called to the benefit obtained from the use of coal tar in infantile eczema; he regarded it as the most useful instrument in his hands; it was such a powerful antipruritic. He preferred weaker preparations of it than those generally used—5 per cent. or 6 per cent. coal tar made up with starch, zinc, and vaseline. Much depended on the quality of the coal tar used, for certain preparations were more reliable than others.

He (the speaker) had seen one or two cases of sudden death in infantile eczema, and had heard of others. The fatality seemed to have been due to chill; the infants had perhaps been injudiciously dressed, cold evaporating lotions having been employed, a procedure resulting in broncho-pneumonia, from which the child had died.

Dr. HALDIN DAVIS

said that those present who were not members of one of the two Sections responsible for this discussion, would probably have been struck by the fact that the views taken on the subject by children's physicians and dermatologists were opposed to each other in every way. The children's physicians did not lay stress on external causes, or concern themselves much with external treatment. The dermatological fraternity, on the other hand, poured mild contempt on the idea of treating eczema by alterations in diet. Both Sections desired to treat the disease as far as possible in a scientific spirit, therefore there must be some explanation for the radical difference of standpoint

revealed. He (the speaker) thought that the reason was that they did not see the same kind of cases. The person who had the "first go" at eczema was the physician, who, when he had tried various forms of dietetic treatment, and found that the patient did not improve, referred the case to the dermatologist. No doubt many babies who were injudiciously fed did present scurvy lesions and spots, which disappeared, after a time, when the diet had been regulated, and the impression gained was that a case of eczema had been cured. But the cases of eczema seen by dermatologists both in hospital and in private practice were of a much more severe nature. He cordially agreed with what preceding dermatologists had said this evening, that it was never possible successfully to treat a frank, well-marked and well-established case of eczema in the infant solely by means of diet or medicine; and that protection and anti-pruritics constituted the sheet-anchor of treatment. He supposed, however, that there was something in the constitution of these children which rendered them liable to be affected by slight irritants in a way that most children were not affected, a peculiarity which was probably an integral part of their constitution, but our knowledge was not sufficiently far advanced to enable us to say definitely what that defect was. Therefore at present we had to rely upon external measures. He (the speaker) had been trying to find whether there was any constitutional defect in these eczematous children with regard to the behaviour of their blood-sugar, i.e., whether there was any abnormality in its quantity and in its variations. He believed some eczematous children had more sugar in their blood than other children had. In one or two children of 3 to 4 years of age, in whom eczema had persisted from infancy, he had found the sugar content of the blood was abnormal, and that if one caused these children to ingest a certain quantity of glucose (50 grm.) the blood-sugar curve did not follow the normal course, but rose more quickly, and required a longer time to fall to the normal.

Dr. MURRAY BLIGH (Liverpool)

said that in Lancashire it was believed, among the poor, that if eczema were cured too quickly, the infants would die. It was a fact that they did so. He (the speaker) had made a post-mortem examination on two children who had died within forty-eight hours of the disappearance of the rash, but nothing was found to account for death; there was nothing abnormal in their lymphatic systems. In a third case there was undoubted pneumonia, and he was sure this disease played a part in most of the fatalities, and particularly in the hydrated child.

He (Dr. Murray Bligh) had never seen typical eczema on the buttocks of a child, though he had seen there many and various erythemata and rashes.

The physician had to be interested in these cases and sometimes had to see them to the bitter end. He would describe the treatment which he (the speaker) employed, and with which he had had more success than with some of the more complicated methods. First, and most important, was a good nurse, one who could properly apply olive oil to the whole body, and keep the affected areas constantly in contact with the oil. The worst cases did not occur so frequently in hospital practice among the poor as among private patients in good circumstances, for whom the whole-time attention of a good nurse should be available. There should be applied three layers of the finest butter-muslin procurable, each saturated with oil, to the area of skin involved, and chloretone in suitable doses should be given to keep the child quiet. As a routine treatment he gave alkalis, mainly because these children developed an irritating condition, not eczematous, on the buttock, which alkali tended to control. Most of the patients had been cured by such treatment in six weeks, and, when the child was being breast-fed, without change of diet. He (the speaker) had never been able to satisfy himself that taking the child from the breast had played any part in producing a cure, but it was true that children who had been fed on patent foods got better when these foods were replaced by whey.

Mr. FRANK COKE

said that he had taken the history of 1,000 cases of asthma and in the whole series 18 per cent. gave a history of eczema. In 500 cases sensitive to foreign proteins, the percentage was 25 per cent. In 250 cases sensitive to foods, no less than 37 per cent. gave a history of eczema.

Many cases of eczema in childhood no doubt were easily cured, but he (Mr. Coke) considered that in any case of eczema, at any age, which was refractory to external applications, the patient should be thoroughly tested for sensitization to foreign proteins.

He would quote one typical case. A child, aged 2½ years, who had been breast-fed until she was 11 months old, began to suffer from eczema immediately after she was weaned. When seen she had eczema all over her body, was swathed in dressings and wore arm-splints to prevent her from scratching.

She gave extensive reactions to cow's milk, goat's milk, eggs and wheat. She was not sensitive to beef, oranges, potatoes or rice. The eczema was cured by discontinuing the foods to which she was sensitive and putting her on a diet of potatoes, beef, rice and oranges.

The blood-count showed an eosinophilia of 40 per cent. at the outset; this had now fallen to 10 per cent. Recently the child got hold of a crust and ate it, and after this a large patch of erythema developed on her face, the skin round the eyes swelling up. This showed that she was still affected by wheat, although her skin was now perfectly clear.

In some cases eczema of the face could be caused by sensitization to feathers.

Apart from the method of avoidance he (the speaker) had cured many cases by non-specific methods, such as collosol manganese or calcium given intravenously, peptone, or the mixed coliform vaccine.

Dr. S. E. DORE

was not disposed to underrate the importance of diathetic and inherited conditions such as asthma, ichthyosis, &c. He also thought that super-alimentation was an important factor in the treatment of eczema in children, and the administration of thyroid gland was often beneficial. He was in agreement with the speakers who laid so much stress on the external causation of infantile eczema. Eczema in infants had been divided by Whitfield into two groups: (1) the simple or traumatic variety, including the intertriginous and septic cases, and (2) the seborrhœic variety. In other words, speaking generally, eczema in infants could be divided into two classes: (1) eczema due to the infant's own secretions, viz., sweat and sebaceous secretion, saliva, vomit, &c., when on the cheeks, and urine and fæces when in the napkin area; and (2) eczema due to the secretions of the mother or nurse, including the seborrhœic variety, which constituted in his (the speaker's) opinion a very large percentage of the cases. The point he wished to emphasize was that seborrhœic eczema, whatever the term implied, was due in many cases to infection from the mother as the result of brushing and combing the hair as well as by direct contact. This type of eczema was generally amenable to local treatment.

Dr. M. SYDNEY THOMSON

said that he agreed with other speakers on the point of external irritation in the infective and facial traumatic types. Some of the cases, however, when first seen, had been persisting for some time and the consequent insomnia and exhaustion had apparently upset the child's digestion; unless that was attended to it was difficult to cure the eczema. For that reason there seemed to be an indication for the more frequent administration of hypnotics than was now usual. He (the speaker) had found small doses of chloral and bromide very useful.

He did not know in what way external irritation could possibly cause the sudden acute eczema which flashed on to the flexures of many children of the plump, carbohydrate type. He (Dr. Thomson) had not had strikingly good fortune in the treatment of that form. He had not seen a case of eczema associated with cyclical vomiting, but he had seen the association of lichen urticatus with the latter condition.

Dr. J. H. SEQUEIRA (Chairman)

said he could congratulate the Members present, as well as himself, on a very interesting debate. The subject of the discussion was really a legacy from his predecessor. He (the speaker) agreed that eczema was not a disease, but a reaction of a particular type of skin. Dermatologists were finding that these reactions were more and more definitely traceable to external causes. As a teacher of dermatology he always thought it his duty to recommend that the question which should be considered when one saw any kind of skin inflammation was: Is this due to some external cause? An endeavour should be made to answer this before one began to think of an internal cause. And that was the point of view which was held by most dermatologists with regard to infantile eczema. It was, however, of great value to the dermatologist to hear so ably expressed the views of the children's physician, who viewed skin affections as expressions of some internal disturbance.

Dr. A. M. H. GRAY (in reply)

said he thought the discussion had been an extremely useful one to all. One point he desired to make clear. He believed that some of his colleagues imagined his (Dr. Gray's) view to be that a diathesis was *alone* responsible for the production of what he called the facial type of eczema. He did not hold that view at all. The view he had always held, and continued to hold, was that what was named eczema was a superficial catarrh of skin—and he reminded Dr. Langmead that those were the words used in his (the speaker's) opening address—which was always caused by an external irritant. But the external irritant might vary enormously both in its intensity and in its character, the intensity of the reaction being not so much the result of the external irritant as of the sensitiveness of the skin. Dr. Adamson thought that friction was sufficient to produce this reaction in any normal infant, a view he (Dr. Gray) did not hold. He held that the children who acquired this facial type of eczema—which he did not think was due to bacterial infection—produced it by friction, but he considered that in those infants there was an underlying condition which could only at present be described as a diathesis.

He thought the meeting was very much indebted to Dr. Cameron for the trouble he had taken to explain so many of those metabolic conditions which were now attracting the attention of the internists, and many of the things Dr. Cameron said would be of extreme value in elucidating this problem of facial eczema.

Another point to which he would refer was that concerning deaths from eczema. He could not help feeling that there was a definite syndrome which was associated with this condition. It was one which was but rarely seen by dermatologists; but cases were definitely described by children's physicians and by dermatologists. An interesting paper had been published by Hudelo and Louet, of Paris, in which the syndrome was described very dramatically and the theories as to causation fully discussed. He (the speaker) considered it to be a very definite state.

Dr. CAMERON (in reply)

said that Professor Langmead and himself seemed to have been in the minority in this debate, and did not secure much support from members of their Section. He (Dr. Cameron) did not wish it to appear that he belittled or failed to appreciate the considerable power which the skilled dermatologist possessed to control the symptoms of eczema. That local treatment was successful in a high percentage of cases was obvious. He was astonished, however, to hear from several speakers that they were not dissatisfied with the present condition of matters. He would have thought that infantile eczema was a disease in which the results of treatment were

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often very disappointing. Again and again he had seen sudden exacerbations at a time when there could have been no local irritation and when local treatment in all its intensity was being carried out. The word "reaction" appeared to have afforded some satisfaction to the dermatologists in the discussion. Without undervaluing the importance of local irritation as an exciting cause, it seemed necessary to ask why *certain* infants should react in this extraordinary way to irritations to which *all* infants were exposed—to scratching, to the cold of winter or the heat of summer. Why, especially, did infants of certain families, of certain stocks, tend to react in this way? If new knowledge of the subject was to be gained, it seemed to him that it must proceed from a close study of the peculiarities of the eczematous infant. He could not agree that the cause of eczema was to be found invariably and solely in different varieties of external irritation.

Sections of Ophthalmology and Laryngology.

Chairman—Sir ARNOLD LAWSON, K.B.E., F.R.C.S. (President of the Section of Ophthalmology).

DISCUSSION ON OPTIC NEURITIS IN ITS RELATION TO SINUSITIS.

(I) CLINICAL CASE.

Case of Cure of Retrobulbar Neuritis following Nasal Exploration.

By R. AFFLECK GREEVES, F.R.C.S.

I THOUGHT this case would be of interest partly because it is one of retrobulbar neuritis, which went on for six months practically unchanged until the nose was explored, and when that was done the patient very rapidly improved, and finally got well; and partly because of the rather unusual permanent effect on the pupil. The pupil, which was formerly three-fourths dilated, is now small, but it has never regained its light reaction. In other respects the eye has absolutely recovered; vision is $\frac{6}{6}$, the optic discs are normal in appearance, and the field, both for colour and for white, is quite restored. It was very striking to notice how quickly the vision improved and how rapidly the pupil commenced to become smaller after the first operation, for she had two operations. At the first the sphenoid was explored by Sir StClair Thomson and the sinus was washed out. After that there was a definite improvement in vision, but the final cure did not take place until the ethmoid had been explored and drained also.

Another point is that a culture was taken and the influenza bacillus was found in pure culture. During the last year I have seen three cases of post-influenzal retrobulbar neuritis; they were mild cases, vision not being below $\frac{6}{6}$, and the condition in all three rapidly cleared up. In each the vision became affected when the patient was convalescing after a definite attack of influenza.

Discussion on Case—Dr. P. WATSON-WILLIAMS asked how long after the onset of the retro-bulbar neuritis the culture was taken; also whether the ocular defects were unilateral. Also, was it a pure culture of the influenza bacillus which was found, or were there other organisms?

Mr. A. L. WHITEHEAD asked whether any vaccine treatment was given.

Mr. J. H. FISHER said it would be interesting to know whether there was cycloplegia as well as iridoplegia in this case.

Mr. GREEVES (in reply) said that this patient had never suffered from cycloplegia. The culture was taken a year after the trouble began. Vaccines were administered after the second operation, and the patient herself considered that she derived very much benefit from them. He understood that only the influenza bacillus was present in the culture; it was taken under the direction of Sir StClair Thomson, who would probably answer that question.

Sir STCLAIR THOMSON said he had the opportunity of seeing this case from the beginning, the lady being on the staff of the Midhurst Sanatorium. In June, 1923, he was told at one of his visits to that institution that this lady had become blind in one eye from retrobulbar neuritis, and his comment

was "That is my job." He proceeded to examine her, but found nothing amiss, and so concluded it was "not his job." In February of the following year, during another of his visits, he was told she had remained more or less blind in that eye, and that she had a deeply seated pain. On looking at her again he still found no symptoms of what was called sinus disease, but as she had become no better in six months, he thought something ought to be attempted. Therefore, in St. Thomas's Home, on February 12, 1924, he made a large opening into the sphenoidal sinus. It was quite healthy, but on the 25th of that month Mr. Greeves reported that there was a definite improvement—the sight, which had been remaining at $\frac{6}{60}$, was now $\frac{6}{6}$, and the pupil, though inactive, became smaller. Her condition was improved but not cured. In July—six months later—he opened the posterior ethmoidal cells. The patient was convinced that her chief improvement dated from the second operation: she lost her pain and throbbing, and Mr. Greeves reported that there was still further improvement after that time. She was given vaccines only because scabbing from the site continued to occur. Dr. Matthews reported that there was a great profusion of influenza bacillus in pure culture. There was still a little scabbing.

The important point about this case was that for six months he (the speaker) neglected her, thinking there was nothing the matter with her. He then opened her sphenoid, which was healthy, and later he opened the posterior ethmoidal cells, and her improvement dated from that time. Previously she had been suffering intensely from a throbbing pain, and this also abated; and though her eyesight improved after the opening of the sphenoid, it improved still more after opening the posterior ethmoids. He thought the vaccine had only been of help in regard to the scabbing. The ethmoid showed cystic degeneration, with muco-pus.

Dr. JOBSON HORNE, speaking with reference to the diagnosis made of post-influenzal optic neuritis and the finding of the influenza bacillus in the discharge from the nose, asked Sir StClair Thomson whether, in this case, the influenza bacillus was regarded as the cause of the optic neuritis, as it had long ceased to be regarded as the cause of influenza.

Mr. A. L. WHITEHEAD said he understood that Sir StClair Thomson did not find a collection of pus in either the sphenoid or the posterior ethmoid cells, only some thickening of mucous membrane. In opening the sinuses, did he remove the posterior end of the turbinal?

Sir STCLAIR THOMSON (in further reply), said he opened the sphenoidal sinus by pushing out the middle turbinal, and making a large free opening into the sinus. There was no pus in it at any time, though the mucosa looked thickened. The posterior ethmoidal cells had no very typical pus in them; when they were opened, what was seen was cystic degeneration and muco-pus. There was, as in many such cases, a little scabbing afterwards. The influenza bacillus was only investigated some months later, and the vaccine was given to try to help get rid of the scabbing and the muco-purulent catarrh.

(II) DISCUSSION.

Dr. A. LOGAN TURNER¹ said that a Conjoint Meeting of the Scottish Society of Laryngology and Otology and the Scottish Ophthalmological Club decided, in March, 1924, to investigate a series of cases of retrobulbar neuritis in regard to the condition of the eyes and the nasal and accessory cavities, and report on them in two years' time; he was able, therefore, to give some of the results in the Edinburgh centre.

His (Dr. Turner's) concern in the present discussion was to speak of twenty-eight definite cases in their rhinological aspect. They all belonged to the retrobulbar

¹ Abstract of opening address.

type of optic neuritis, and the natural tendency was for the vision to recover spontaneously. This was the end-result in most of the cases examined. Some operators, he said, showed an excess of zeal in interfering with the nose and sinuses in these cases, under the belief that "latent sinusitis" was the cause of many of them. In the cases under review there was almost complete absence of any subjective nasal symptom. In two, a slight unilateral nasal obstruction was found to be due to a septal deflection, whilst in none of the cases did rhinoscopic examination reveal the signs which the rhinologist regarded as evidence of suppurative sinus disease. In thirteen of the cases the nasal cavities were normal. In seven there was a high septal deflection to the side of the affected eye, two of these showing some cloudiness of the sphenoidal sinus in the skiagram. In five cases a high septal deflection was associated with œdema of the middle turbinal on the same side. In three of the patients the nose was not examined.

Dr. Turner concluded with a general summary of the facts gleaned. In none of the twenty-five cases nasally examined was there clinical evidence of suppurative sinus disease, and in the six cases in which posterior sinuses were opened, no pus or secretion was found. In these six the cavities were healthy in three, the remainder showing slight catarrhal changes and some evidence of congestion of the mucosa. In two cases a septal operation was carried out. In all the cases of deflection the vision returned to normal or nearly normal. In three of the patients septic teeth were a possible causal factor, and after they had been extracted, vision was restored. Dr. Turner said that in estimating the effect of surgical interference with the sinus cavities on the vision, due regard must be had to the fact that in these cases the tendency was towards spontaneous cure, and the operation might synchronize with the time of commencing natural resolution. A further collective investigation on the subject was needed.

Mr. M. S. MAYOU: The relationship between diseases of the nasal sinuses and diseases of the eye is now so well recognized that most ophthalmic hospitals have a rhinologist attached to their staffs; I believe that the Central London Ophthalmic Hospital to which I am attached was the first eye hospital in London to make such an appointment. We therefore have had for a considerable period the benefit of a skilled examination of the nose in cases of optic neuritis of doubtful origin.

The forms of optic neuritis associated with nasal disease fall into two main groups which exhibit entirely different clinical and pathological characteristics.

First, papilloedema, or swelling of the nerve-head, which is due to distension of the optic nerve sheath with fluid, causes venous obstruction by pressure on the central retinal vein at its entrance into the globe. The distension of the sheath may occur either as the result of increased intracranial tension, or, in rare instances, as the result of inflammatory exudation from the dural, pial, or arachnoid membranes of which it is composed, either as a spread of inflammation from the meninges, or a local patch of inflammation in the sheath of the nerve. The principal clinical signs to which it gives rise are a slow, steady failure in vision; very marked swelling of the nerve-head and intense congestion of the retinal veins often with hæmorrhages and white patches of exudation into the retina, a condition known clinically in the advanced stages as "choked disc."

Secondly, retrobulbar neuritis. A much better term would be "interstitial" neuritis, for, if the inflammation occurs in or spreads to the area in which the central retinal vessels are present in the nerve, there is a visible optic neuritis at the disc. In this disease there is an inflammatory patch or patches; there are inflammatory exudations into the trabeculæ of the optic nerve, causing direct pressure on the nerve fibres and interference with their function, and in some cases bringing about their complete destruction. The nerve bundles first affected by pressure are those from the region of the macula, since these are more highly

specialized in function, and therefore more vulnerable; but in rare cases, if the patch of inflammation causes destruction of certain nerve bundles without producing much pressure-effect within the nerve, we may get scotoma elsewhere in the field than the macula. The principal cause of the disease, and the only one of which we have positive evidence, is disseminated sclerosis, in which we have patches of an inflammatory degenerative process occurring in the nerve; but it is probable that similar patches of inflammation may occur from embolic infection through the blood-stream, from a septic focus elsewhere in the body, such as a suppurating sinus in the nose. As an analogy of this form of infection in the eye itself we have cases of chronic irido-cyclitis, scleritis, and choroiditis of septic, syphilitic and tuberculous origin.

The principal clinical signs of the disease are a rapid loss of central vision, the characteristic pupil reaction to light, in which, after a maximum contraction, the pupil dilates with marked hippus, and a tenderness on movement, or pressure of the globe backwards into the orbit, a central scotoma for white and colour, and sometimes limitation of portions of the peripheral field.

All the physical signs of retrobulbar neuritis may be produced by pressure on the nerve by a tumour, fracture of the sphenoid, or inflammatory swelling in the neighbourhood of the optic foramen, without the nerve substance being involved. By far the most common cause, judging from the literature, is a syphilitic periostitis in the neighbourhood of the optic foramen, and it is quite possible, in rare instances, that the inflammation of the sphenoidal sinuses and posterior ethmoidal cells may cause direct pressure on the nerve and so produce the physical signs of retrobulbar neuritis without being, pathologically speaking, true inflammations within the nerve sheath.

We now pass to the most important part of this discussion, namely, the relationship of the nasal sinuses to optic neuritis. Papilloedema may occur as the result of a subacute meningitis following a suppurating sphenoidal sinus opening beneath the dura, or a spreading necrosis of the cranial bones, as the result of operation on, or disease in, the bones of the nose, and, in rare instances, as the result of thrombosis of the cavernous sinus.

The papilloedema, in the case of subdural rupture of the sphenoidal sinus, may be present for a very long time before the cause is discovered. In this connexion it is of considerable interest that the first case recorded in the *Transactions of the Ophthalmological Society* of sphenoidal sinus disease associated with optic neuritis, in which a full post-mortem examination was made, was one in which there was double optic neuritis of the papilloedema type [1]. This existed for two years before the death of the patient, and it was not until the last two months of his life, when proptosis also began to show itself, that the cause of the neuritis was suspected. At the post-mortem examination it was found that there was a subdural abscess beginning in necrosis of the walls of the sphenoidal cells which pushed upwards the optic nerves and commissure and tracked outwards subdurally across the middle fossa. Post-mortem examinations are so rare in sphenoidal sinus disease that this case is of special interest, showing that papilloedema was produced, not the interstitial neuritis generally supposed to be associated with this disease.

Recently a case of papilloedema associated with sphenoidal sinus disease has also been reported by Wright [2].

If one looks at the beautiful collection of specimens made by Professor Onodi, and at present in the College of Surgeons Museum, one sees that the optic foramen is only in relation to the sphenoidal sinus at its lower and inner part. The thickness of bone forming this part of the canal varies very considerably in individual cases; in many cases it is quite thick, but, even when thin, in practically no instance is it the thinnest part of the bone which forms the wall

of the sphenoidal sinus, and therefore if the sphenoidal sinus became distended this is not the part which is likely to yield and cause pressure on the nerve. Some authorities look on interstitial neuritis as the direct spread of the inflammation from the sphenoidal sinuses to the interstitial tissues of the nerve, but it is very difficult for me to believe that this spread takes place. We have not only the barrier of bone and periosteum, but also the three layers of the sheath of the optic nerve, and although it may be possible that some emissary veins may anastomose in the sheath of the dura, it is extremely unlikely that inflammation will be able to overcome the resistance of the other membranes covering the nerve. That the resistance of the nerve sheath is great is seen in tumours of the orbit, where the nerve sheath may be completely surrounded by the tumour, but the nerve is not invaded by the tumour cells; also in cases of orbital cellulitis, in which the nerve may be literally bathed in pus and yet symptoms of interstitial neuritis are never present.

In the case of suppuration in the sphenoidal sinus already quoted, the optic nerve actually lay in contact with a subdural abscess probably for nearly two years, yet interstitial neuritis was not produced and there was merely an œdema of the nerve-head due to increased intracranial tension.

Having dealt with the anatomical and pathological factors, we must now pass to the clinical evidence of the association of nasal diseases with neuritis. The papillo-œdematous type of optic neuritis in association with meningeal infection and intracranial abscess is recognized by everybody. It is with the relation of the interstitial or so-called retrobulbar type to nasal disease that we are particularly interested.

StClair Thomson [3], Mackay, Risley [4], De Schweinitz [5], Holmes, Birch-Hirschfeld [6], and other observers have recorded cases of recovery of interstitial neuritis after the evacuation of the sphenoidal sinus, but in cases of interstitial neuritis, except in rare instances, there is a strong tendency to recover, whether any form of treatment is given or not. Therefore, if a sphenoidal sinus is opened and the patient recovers, it is not certain that the recovery is the result of operation; indeed in two of my own cases of bilateral retrobulbar neuritis, in which the patient went completely blind, and no recovery took place, the sphenoidal sinuses were opened and nothing was found. It is possible that more light might be thrown on the association of the two diseases if a methodical examination of the fields of vision were made in a series of cases of sphenoidal sinus disease. Wallis [7], who examined forty-five cases of sinus disease, found a general contraction in all. Ten cases showed temporal contraction, of which seven were bitemporal and one a case of bitemporal hemianopsia. Central scotoma was observed five times and optic neuritis was present in three of them. I think one must be a little careful in accepting accounts of concentric contraction of the fields, as I do not think it is the general experience of ophthalmic surgeons, but more accurate observations of this kind are required.

I have had a considerable number of cases of retrobulbar neuritis examined by rhinologists, but they have never yet found one where the sphenoidal sinus was infected. On the other hand, I have had three cases in which the antrum has been full of pus and one case in which the ethmoid was infected. After opening the antrum and clearing out the ethmoid, in all these cases the patients made a satisfactory recovery.

To summarize: The papilloœdematous type of optic neuritis may occur as the result of infection of the meninges from the nose, or increased intracranial tension as the result of an intracranial abscess and cavernous sinus thrombosis.

Interstitial or retrobulbar neuritis probably never occurs as the result of direct spread of infection to the nerve, but may be caused by embolic infection through the blood-stream, from a septic focus elsewhere in the body as, e.g., from an infected nasal sinus. The symptoms of retrobulbar neuritis may be produced by external pressure

on the nerve in its passage through the foramen as the result of distension of the sphenoidal sinus, or of periostitis in the neighbourhood of the foramen.

The association of the two diseases is rare, but of undoubted occurrence.

REFERENCES.

- [1] SANFORD, A. W., *Trans. Ophth. Soc. Lond.*, 1894, xiv, p. 119. [2] WRIGHT, R. E., *Brit. Med. Journ.*, March 28, 1925. [3] THOMSON, STCLAIR, *Brit. Med. Journ.*, June 2, 1925. [4] RISLEY, *Annals of Ophth.*, October, 1908, p. 608. [5] DE SCHWEINITZ, *Trans. Amer. Ophth. Soc.*, 1910, Ohio States, New York. [6] BIRCH-HIRSCHFELD, *Klin. Monatsch. f. Augenheilk.*, January, 1908, p. 1. [7] WALLIS, F. C., *Proc. Roy. Soc. Med.*, 1911, iv (Laryng. Sect.), p. 165.

Mr. E. D. D. DAVIS: I have studied the notes of seventy-six cases of retrobulbar neuritis sent to me by ophthalmologists for an examination of the nose with a view to ascertaining the cause of the condition of the eye. The patients were kept under observation for long periods and the cases were followed up. After repeated nasal examinations, with a thorough investigation of the ætiology of each case, the following results were obtained:—

Syphilis	9
Disseminated sclerosis	14
Pituitary tumour	2
Choroiditis	2
Leber's optic atrophy	1
Lead poisoning	1
Tobacco and alcoholic amblyopia	1
Albuminuric retinitis	1
Septic teeth	7
Embolism	3
Manifest nasal sinus suppuration	5
No cause ascertained but nasal disease excluded	30

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Syphilis as a cause of the neuritis was easy to diagnose because there were other signs of syphilis and a positive Wassermann reaction, but in two of the nine cases nasal sinus suppuration co-existed, though it was subsequently proved that the syphilis, and not the sinus suppuration, was the cause of the neuritis. On the other hand, E. B. Fink, of Chicago, records in the *Journal of Surgery, Gynecology and Obstetrics* for November, 1925, complete post-mortem and histological details of a case of syphilis in which there had been right optic neuritis and atrophy, following suppuration of the posterior ethmoidal and sphenoidal sinuses, with necrosis of bone, pus in the orbit and within the optic sheath, producing softening and destruction of the nerve, and finally cavernous sinus thrombosis. This case is quoted because it clearly shows how optic neuritis arose from nasal sinus suppuration. Syphilis, plus suppuration of the posterior nasal sinuses, is the most likely cause of optic neuritis, and it is also important to remember that suppuration of the posterior nasal sinuses may be an ætiological factor in syphilitic optic neuritis.

The definite diagnosis of disseminated sclerosis was most difficult because retrobulbar neuritis is often the first and only sign of this disease for many years, but, by a process of exclusion after the lapse of time, and with the aid of the neurologist, fourteen of the cases were found to be due to this cause. The neuritis was unilateral in nine and bilateral in five, and in some there was from time to time a considerable variation in the amount of loss of sight. It is possible that some of the reported cases of the return of vision after a nasal operation in which little or no nasal disease was found are really cases of disseminated sclerosis during the period of improvement, though it is true that in other cases of this type the loss of vision remained stationary and pallor of the optic disc supervened.

The anatomical relations of the sphenoidal and posterior ethmoidal cells to the optic nerve are familiar, and skilfully shown by these photographs and specimens prepared by Professor Onodi. (Photographs and specimens shown.)

These specimens have been especially selected to show how close a relation may exist between the optic nerve and nasal sinuses, but there is a very wide variation in different subjects and a considerable amount of tissue may separate the nerve from the sinuses, more particularly in young subjects, owing to the fact that the sinuses increase in size with age and growth. The Onodi specimens are perhaps exceptional rather than normal.

In addition to the muco-periosteal lining of the sinuses and varying thickness of bone the optic nerve is protected by its sheath of dura mater and brain membranes. The dura mater is an effective barrier to infection, a fact frequently shown in cases of mastoid suppuration in which it is quite common to find the dura exposed by suppuration but having effectively prevented extension to the brain.

Optic neuritis arising from inflammation of the nasal sinuses could be produced by:—

- (1) Direct extension through continuity of structures.
- (2) Thrombosis of venous sinuses or vessels.
- (3) Acute nasal catarrh (Fuchs).
- (4) Toxæmia or bacteriæmia.

Direct extension from the ethmoidal and sphenoidal sinuses was the cause in four of the cases I have seen and in a number of other recorded cases, but it will be evident from the anatomy that the inflammation must be severe and destructive, and this is confirmed by Onodi's collection of nine cases of optic neuritis definitely resulting from nasal sinus suppuration proved by post-mortem examinations on cases in which periostitis, osteitis, and necrosis existed. The pathological details of these nine cases, all recorded by different observers, are given in Onodi's book, "The Optic Nerve and the Accessory Sinuses of the Nose." The disease in these cases was extensive and destructive and accompanied by meningitis, extradural abscess, or venous thrombosis. It is a striking fact that, though severe nasal sinus suppuration is so common, yet it is rarely complicated by retrobulbar neuritis. Flatau records twenty-six cases of sphenoidal sinus suppuration with no affection of the optic nerve, and there are other similar records. This phenomenon can be explained by the strong barrier which exists between the nerve and the nose or by the variation in their relations.

From what has been said above, it will be seen that when optic neuritis is due to inflammation of the nasal sinuses, the disease is easily discovered during a nasal examination and is obvious, and this statement is supported by the five cases which I have seen, and by the reports of cases in which the evidence of extension from the nose is conclusive. In fact, the clinical cases indicate a chronic nasal sinus suppuration in which an additional acute or subacute attack has caused the eye complication. The majority of these cases are unilateral and the sinus disease is on the same side as the nerve affected, but it will be seen from the anatomical specimens that both nerves can be affected, or the focus of disease may be contralateral.

It will be noticed that in only five cases out of 76 was there nasal sinus suppuration. Four cases underwent operative treatment in which the middle turbinal was removed and the sphenoidal and posterior ethmoidal cells were opened. The fifth case was exceptional, because the patient had acute suppuration of the frontal sinus with an orbital abscess and threatened meningitis, and required an emergency operation. After his recovery a post-neuritic optic atrophy with complete blindness was discovered.

The operative treatment in three of the cases produced a dramatically rapid improvement in the sight, and in the two remaining cases the lack of improvement was due to optic atrophy. The lesion was unilateral and the cause was suppuration of the posterior ethmoidal and sphenoidal sinuses. The maxillary antrum was also affected in three of the cases, but it must be remembered that the antrum is a

cesspool for the nasal sinuses and I believe in those cases in which optic neuritis or retrobulbar neuritis have been recorded as the result of antral suppuration, the ethmoidal cells were probably involved and that the disease in this latter region was the real cause of the inflammation of the optic nerve.

Suppuration of the antrum of nasal origin is practically always accompanied by suppuration in other sinuses, such as the frontal and ethmoidal. On the other hand, where antral suppuration arises from the teeth this cavity alone is involved, and optic neuritis or retrobulbar neuritis has never been recorded in such cases, nor have I seen it in the large number of dental cases which I have had under my care. Moreover, the anatomical position of the antrum makes it difficult to understand how suppuration in that cavity can affect the optic nerve; but at the same time it must be admitted that the indefinite condition "toxæmia" cannot be excluded. In these cases and in others recorded in which there was no doubt that the optic neuritis was caused by the nasal condition, the nasal disease was obvious. There was a history of an offensive discharge from the nose, of long duration, and the presence of suppuration and cedema was easily recognized during an examination. This type of neuritis quickly progresses to optic atrophy and permanent blindness, and the sooner the nose is treated the better. The improvement in the sight after operation in these cases was rapid and was confirmed by the ophthalmic surgeon. It was also permanent, the patients being kept under observation for more than twelve months.

The condition of the eye was described by the ophthalmic surgeon as optic neuritis, i.e., there were definite changes in the optic disc, optic atrophy soon followed, and the degree of loss of sight amounted to almost complete blindness. In this respect the nasal cases differ from those due to so-called idiopathic retrobulbar neuritis, in which changes in the disc were absent or very slight, and the loss of vision varied from mistiness to inability to read. The fields of vision in the nasal cases showed an absolute central scotoma, but there was no tenderness of the globe of the eye on pressure or on movement; in one case there was slight exophthalmos.

The suggestion has been made that the charts of the field of vision may help in the diagnosis of the cause of loss of sight. The delicate papillo-macular fibres which supply the macular region lie to the temporal or outer side of the nerve, away from the nose, and in cases of central scotoma it is these fibres which are involved. The periphery of the field of vision is supplied by the fibres which lie in the centre of the nerve trunk. The charts of the fields of vision in the nasal cases showed a large central scotoma; the other so-called idiopathic retrobulbar cases demonstrated a definite contraction of the field and also a central scotoma. Unfortunately, there are so many factors in perimetry which influence the charts that it is impossible to show that only the outer fibres were affected in the nasal cases and all the fibres of the nerve in the idiopathic cases; further, the extent and severity of the neuritis must vary considerably in the different cases. It was hoped that the charts of the field of vision of the nasal cases would show definite characteristics and so be an aid to diagnosis, but on discussing the charts with Mr. Basil Lang, who has made a special study of perimetry and scotometry, it was decided that no such simple conclusion could be drawn, nor was there any probability that such a distinction could be made by the perimeter.

Optic neuritis arising from *septic venous thrombosis* is rare, and the acute illness of the patient overshadows the symptoms of blindness.

Fuchs' observations lead him to think that acute retrobulbar neuritis with central scotoma frequently occurs after *nasal catarrh* and influenza, and rhinological examination may give negative results. Hyperæmia and swelling of the nerve-sheath affect the peculiarly vulnerable papillo-macular bundle, and the condition clears up as it does in the nose and normal function is restored.

I have not seen any cases of retrobulbar neuritis occurring during acute nasal

catarrh or a cold, in spite of the fact that observation of cases of acute catarrh is an everyday experience. In some of the cases in which no cause for the neuritis was found, the patient made the statement that the sight improved during a cold. Others developed colds during the period they were under observation and there was no additional loss of sight nor were there any symptoms to indicate that the condition was in any way aggravated.

Toxæmia and bacteriæmia as causes of optic neuritis are not easy to prove and all I can say is that I have not seen any cases due to the toxæmia of a nasal sinus inflammation or suppuration.

It has been claimed that some of the thirty cases of retrobulbar neuritis for which no cause could be determined were due to a latent nasal sinus inflammation which could not be discovered; for this reason particular care was taken to exclude nasal disease by repeated examinations with exploration of the sphenoidal sinuses and antra. In three of these cases the middle turbinals were removed, the sphenoidal and ethmoidal sinuses were opened and found to be normal and there was no improvement in the sight as the result of this procedure. In two other cases the nose was not above suspicion, and as there was no improvement the sphenoid and ethmoid were opened and found to be absolutely normal. Both these cases ultimately turned out to be disseminated sclerosis in which the sight varied, as in other cases due to the same cause.

In nearly all the thirty cases, X-ray examination, Wassermann reaction, tests of the urine and of the nervous system and searches for tuberculosis invariably gave negative results, neither was there any evidence of toxæmia, and though the patients were seen at intervals, over a period of more than twelve months, no further information as to the ætiology was obtained. Nevertheless fourteen patients recovered, the condition of five was stationary; the remaining eleven showed no change while under observation, but they cannot be traced and the final result could not be obtained.

It is possible that if in the fourteen cases which recovered the ethmoid and sphenoid had been opened, or septic teeth had been extracted, the recovery would have been attributed to the operative procedure. In at least four of the cases of disseminated sclerosis, the cause of the neuritis was at first obscure, but the lapse of time furnished the diagnosis. The examination of the cerebro-spinal fluid in one case was normal and did not assist in making a diagnosis.

In conclusion, if the retrobulbar neuritis is increasing and every other cause for the condition is eliminated, or if there is the slightest suspicion of sphenoidal or ethmoidal disease, then it would be justifiable to remove the middle turbinal and explore the ethmoidal and sphenoidal cells. The risk of damage by an experienced operator in such a procedure is negligible.

Mr. R. FOSTER MOORE said he would confine his observations as strictly as possible to cases of retrobulbar neuritis.

The outstanding characteristics of the disease, as generally understood, were as follows: rapid loss of central vision; some pain on movement of the globe, or on pressing it back into the orbit; an optic disc which was but little removed from the normal in appearance; a pupil which contracted to light but whose contraction was not maintained; and a marked tendency to recovery. The affection was commonly unilateral and occurred most often between the ages of 20 and 40.

It was very striking to observe from literature how prominent a rôle was attributed by some observers to infection of the paranasal sinuses as a cause of retrobulbar neuritis; indeed, one might well be led to believe that this was one of the most important causes of the condition; in his own experience it was quite one of the rarest ætiological factors.

With a view to as complete an investigation as possible he admitted all his cases as in-patients so that they might be thoroughly investigated by a neurologist—

either Dr. Hinds Howell or Dr. Gordon Holmes. Skiagrams were taken. They were referred to the dental department, the Wassermann test was applied and the urine examined, and the sinuses investigated.

No doubt that two factors had contributed to the association of retrobulbar neuritis with paranasal disease; first, the close relationship of the optic nerve to the sphenoidal sinus had led to the expectation that the nerve might readily be involved in disease of it; and secondly, some observers had failed to remind themselves of the common course of the disease, namely, that recovery of sight was the rule and that frequently it was rapid, so that should an operation on the sinus or any other treatment be carried out while the sight was greatly reduced, improvement was exceedingly likely to follow. Unless the ordinary course of the condition was remembered the improvement of vision was likely to be attributed to the operation.

Some observers believed that a latent sinus infection might often be the cause of the condition, a suggestion probably based upon the observation that many cases recovered after the sinuses had been opened; but this attitude required an especially critical consideration before it was accepted. He suspected that there were very few of these cases which would not have got well had nothing been done. After one had exhausted all forms of investigation which seemed to hold out any prospect of revealing the source of the trouble, there was left a large group in which he thought the real cause remained undiscovered.

We were greatly indebted to Mr. Davis for the critical care with which he had analysed his seventy-six patients and the pains he had taken to follow them afterwards. It would be noticed that amongst them he found fourteen cases of disseminated sclerosis, and most likely he (Mr. Davis) would agree that in the course of years a considerable proportion of those thirty in which no cause was ascertained would come to be included under this head. It was well known that in many cases of disseminated sclerosis retrobulbar neuritis was the first and, for the time being, the only discoverable sign, and it might be many years before any further manifestations of the disease of the nervous system showed themselves.

Without doubt the optic nerve might be seriously involved by a suppurative process extending to it from any of the surrounding structures, and Mr. Davis had made it clear that the inflammation in such cases was severe and destructive, and was apt to be accompanied by such complications as meningitis, extradural abscess, or venous thrombosis, and, what was important in the present connexion, to give rise to intranasal changes which were unmistakable and readily identified. In some of these cases blindness had resulted from thrombosis of the vessels in the orbit in a way similar to that in which inflammation spreading backwards in facial erysipelas might bring about the same result. Although in such instances the term retrobulbar neuritis, used in its anatomical sense, might be applicable, it would not, he thought, generally be used clinically in this way.

In conclusion, he would say that, apart from the spread of a suppurative process from surrounding structures, which had given rise to an orbital abscess or thrombosis of the vessels—cases which few clinicians would include as instances of retrobulbar neuritis—he had never seen a case of retrobulbar neuritis which he believed was due to paranasal sinus disease.

If it was a cause of the condition it was a very rare one, and in this view he was fortified by the opinion of six of his colleagues.

Sir STCLAIR THOMSON said that he had had three cases within recent years, and he called to his support in regard to them Mr. Treacher Collins, Mr. Doyne, and Mr. Affleck Greeves. One of the patients had been shown to-day. She had had no symptoms pointing to sinus disease when carefully examined. She had had six months since the beginning of the disease in which to make a spontaneous recovery but she

had not recovered. The sphenoidal sinus was opened, and though it had appeared to be healthy, the patient had improved immediately to some extent. Later, he (the speaker) had opened the posterior ethmoidal cells; they were not actively suppurating, but showed cystic degeneration. After the operation they secreted again. The patient definitely improved and was now quite well.

The next case he (Sir StClair) had seen with Mr. Treacher Collins, and in that case there was no doubt that the patient had pus in both sphenoidal sinuses. He (the speaker) had opened them on December 2, and on December 8 Mr. Collins reported that vision had considerably improved; on the twentieth of that month there was greater improvement, and by January 2 there was complete restoration of vision. That patient went on secreting pus from both sphenoidal sinuses for some time, and finally made a complete recovery.

The third case was under Mr. Doyne and Mr. E. D. D. Davis. The patient was a relative of his (Sir StClair's), therefore he declined to operate on her. She was walking along the street last January, after having had influenza, and she was unable to see the lamps on one side of the street. She was under the care of Mr. Doyne, and there was no suggestion of sinus trouble. She had a deviated septum, and he handed her over to Mr. E. D. D. Davis, who opened the sphenoidal and the posterior ethmoidal sinuses, and resected the septum, but she was still more or less blind in one eye; she had not yet recovered.

As to the future, what would help the profession? Rhinologists could not always tell when pus was present in the sinuses. In cases in which operation was performed the patients recovered, but operation was not always done. He had listened with great respect to what Mr. Foster Moore had said when he impressed upon the meeting that he did not think the sinuses, in many cases, were at fault. He understood that 50 per cent. of the cases recovered without treatment.

Mr. E. TREACHER COLLINS said the case mentioned by Sir StClair Thomson was not one which could be classed as retrobulbar neuritis, as there was marked papillitis. There was not only considerable swelling of the optic disc, but there were patches of exudation on the retina. He saw the case before Sir StClair's operation, also several times afterwards, and there was no doubt about the improvement which it produced, not only with respect to vision, but also in causing subsidence of the swelling of the optic disc and disappearance of the exudation in the retina. He could not recall having seen a case of acute retrobulbar neuritis which could be attributed to sinus disease, but he had seen two or three cases such as Sir StClair Thomson described, in which papillitis was associated with nasal sinus disease, and in which improvement occurred after those sinuses had been tapped and washed out. He long ago gave up advising nasal sinus treatment of cases of retrobulbar neuritis, but when there was papillitis or swelling of the end of the nerve, in a case in which intracranial trouble and syphilis could be excluded, it might be due to sphenoidal or ethmoidal sinusitis, and exploration of the sinuses might be justified.

Mr. F. A. WILLIAMSON-NOBLE said there was a small point of interest in the aetiology of retrobulbar neuritis, namely, the size of the optic foramen. As far as he remembered, in most cases of retrobulbar neuritis there was a smaller optic foramen than normal. That suggested that one of the explanations of the condition might be that it was due to pressure on the nerve. It had also been suggested that in some intractable cases it might be possible, by the subperiosteal route, to reach the optic foramen and enlarge it.

Dr. P. WATSON-WILLIAMS said that it was very interesting to him to hear that retrobulbar neuritis showed such a marked tendency to recovery. Yet he had been led to believe that notwithstanding such a tendency, a considerable number of cases progressed, and a certain proportion ended in optic atrophy—a very disastrous

happening for the patient. It was therefore all-important that no stone should be left unturned which afforded any probability of yielding a successful result. One of the cases mentioned that night indicated the importance of making a careful ophthalmological examination before interfering with the nasal sinuses in cases in which a nasal origin was suspected. Every now and again one met with patients who became partially or even completely blind in one eye without being aware of the fact, and it would be unfortunate if the operation underwent the discredit of having caused such partial or complete blindness as existed previously. He recalled a case of his own in which no blame was attached, but the condition of the nasal sinuses had been investigated just before the eye condition was inquired into; it was then discovered that there was old-standing optic atrophy in one eye, which of course was blind.

Another point of importance to be borne in mind was, that despite the fact that a certain number of cases of retrobulbar optic neuritis recovered—and it was equally true that a considerable number of cases of sinusitis got well spontaneously—there remained a considerable number in which recovery did not occur. In this connexion Sir StClair Thomson's case was of very great interest because it was of the type which emphasized the fact that a nasal sinus condition which did not declare itself by symptoms and which was not to be detected by ordinary methods of examination, might nevertheless be due to nasal sinus infection. And he believed there was no doubt that in the cases of paranasal sinus infection in which there was such absence of marked evidence of suppuration, toxæmic conditions were more likely to arise. It was true that when there was marked suppuration, the more profound pathological changes might cause retrobulbar neuritis, but it was equally true that there were a large number of cases—probably the larger proportion—in which the ordinary symptoms associated with these infective conditions in the sinuses were absent, namely, latent or non-manifest cases. He thought it was because there was such a relative paucity of polymorphonuclears that absorption of toxin was more likely to occur than in cases in which there was a profuse outpouring of pus. And sometimes there was great difficulty in investigating these cases of suspected sphenoidal or posterior ethmoidal infections. He had recently published in the *Lancet* two cases which were of profound interest, as they well illustrated how easy it was to overlook the existence of suppuration when these sinuses were infected. One was a case in which there was a large sphenoidal sinus infected, and a relatively small sphenoidal sinus on the other side. Examination led him to think that both sinuses were infected, because pus could be extracted from the sphenoidal sinus on both sides. But he proved that he had entered the same large cavity twice, as it was extending well across to the opposite side, this accounting for the eye on one side only showing evidence of retrobulbar neuritis, while the small, ill-developed sinus on the other side was not infected, and the corresponding optic nerve had escaped.

The second case was one in which a skilful colleague explored the sinuses with negative results. He (the speaker) remembering the first case, explored in the special way he used in order to discover a small sinus, and he found in this case that while the large sphenoidal sinus was free from infection, the relatively small sinus was infected, and improvement in the nearly blind eye quickly set in when the real seat had been discovered. He could not regard it as merely a coincidence, for the patient had previously had a long time in which to get the benefit of treatment, and to receive any benefit due to the lapse of time.

He therefore suggested approaching all these cases with an open mind, remembering that it was the cases in which manifest sinus suppuration was almost absent that one was apt to find the source of the trouble. Often it was the ethmoidal cells which were involved; indeed they seemed to lend themselves, by their anatomical relationships, to lymphatic absorption involving the optic nerve sheath, and it might

be that infection of the optic nerve from sphenoidal sinus infection might take place just anterior to the sphenoidal sinus, in the sphenothmoidal fissure. But it must be recognized that there were many other conditions, apart from those in the nose, which might be answerable for retrobulbar neuritis, and without a definite sinus infection the ocular lesion could not be rightly attributed to nasal sources.

Mr. J. A. GIBB (Maidstone) said he was connected with a hospital in which there was an ear and nose and an eye department, and there was a fairly close liaison between the two. His colleague, when he reached a stage at which he failed, sent the patient to him (the speaker) in the hope that he would be able to do him some good.

During the last three years he had had eight definite cases of retrobulbar neuritis referred to him for observation and necessary action. In this he had proceeded on the lines laid down by Dr. Logan Turner and Dr. J. S. Fraser, i.e., if observation made clear to him that the nasal sinus was infected the treatment should be directed to the sinus or group of sinuses affected. In the first five cases of retrobulbar neuritis, with scotoma mapped out by ophthalmic surgeons, the anterior ethmoidal cells were definitely infected. He did what he was taught to do by Mr. Waggett, i.e., to note the directional flow from the sinuses, especially the postnasal appearance of discharge. He operated entirely on the anterior ethmoidal cells, and the patients in those cases recovered completely. They were cases in which the optic neuritis had been in existence some weeks.

In the other two cases there was double retrobulbar neuritis; one patient had reached the stage of optic atrophy in his right eye, and his left optic nerve was still actively inflamed. In both the condition of the nose pointed to posterior ethmoidal disease and sphenoid disease. One of the men had retinitis, and his urine was loaded with albumin. The Wassermann test was applied to the cases in order to put syphilis out of court; it was absent. This proceeding was always difficult because it was such a common practice in the eye department to give iodide of potassium, and that tended to mask a true Wassermann result. In the albuminuric case the optic neuritis in both eyes completely cleared up in a fortnight, and the patient left the hospital with his urine clear of albumin as well. In the other case, however, the operation on the posterior ethmoidal cells and sphenoid had no effect at all, and at the end of a fortnight he found that the sphenoid opening had completely closed up. In that case he (the speaker) suspected syphilis, because that rapidly caused adhesions. Punching the sphenoid open had no effect on the sight. He sent that patient away to a convalescent home for a month, and when he returned his vision was worse. The patient agreed to the speaker's suggestion that a further operation on the nose should be done, and he (Mr. Gibb) then opened the anterior ethmoidal cells and thoroughly burred the maxillary antrum, which contained pus, and after that there was a steady improvement, vision increasing from $\frac{6}{60}$ to $\frac{6}{18}$.

Mr. LEIGHTON DAVIES: In my experience visible changes in the optic nerve in cases of nasal sinus disease are relatively uncommon. Retrobulbar neuritis of the classical type is also not common. But I want to place before you some observations regarding the visual fields in cases of nasal sinus suppuration which may be of some value in elucidating the way by which the optic nerve is involved in cases of chronic nasal sinus disease; I leave the acute cases out of account for the moment.

In taking the visual fields in these chronic cases I have been struck by the fact that in the great majority I have found definite changes present. These changes may be: (a) Peripheral, or (b) central, i.e., enlargement of the blind spot or scotomata of various types may be present; and (c) we may find both types together.

Now, by far the commonest changes are those involving the periphery of the visual fields, producing contraction. I find that this is a very constant accompaniment of chronic nasal sinus infection. This contraction is usually concentric, and involves white as well as colour fields—though the latter are contracted proportionately to a greater degree than the white field. It invariably affects both eyes, though not necessarily to the same extent, and it may attain a very marked degree, though without in any way affecting central vision. I have charts showing white fields down to twenty degrees or less.

Usually in severe cases these fields tend to become smaller until the sinuses have been opened and drained, but if they are markedly contracted and the sinus disease has been of long duration, they seldom regain their full size and very often do not improve at all.

The fields for blue always enlarge to a greater extent, and more rapidly than those for red or green. Such cases as these, even where the contraction is extreme, are never likely to become blind if the visual acuity is good, unless an acute retrobulbar neuritis supervenes—a sequel I have not encountered. On the other hand, where an extremely contracted field is associated with loss of visual acuity, I regard the outlook as serious and foreshadowing definite optic atrophy.

Pathogenesis.—What is the nature of the lesion which produces these changes in the visual fields?

I would first draw attention to the fact that these cases are always bilateral, and this suggests that we are dealing with a toxæmic condition, the toxic element being carried by the blood-stream. It may be that the toxin passes directly into the blood-stream from the mucous membrane of the sinuses which is abundantly supplied with venous channels. But there is another possibility; the discharge, which is so common a symptom in every sinusitis, is in large part taken into the stomach where the toxins may gain the blood-stream, unless, of course, they are destroyed by the gastric secretions.

There are these two ways in which the toxin may reach the eye or visual apparatus, and there exhibit its injurious action. If it is true that the toxins act by way of the blood-stream and not directly upon the optic nerve, then it ought to be possible to find contraction of the visual fields in cases of chronic suppuration in which parts of the body other than the nasal sinuses are involved.

With this object in view I have examined a few general and surgical cases of chronic suppuration, but have not yet had the time to collect a sufficient number to afford proof of the truth or fallacy of my supposition. I have examined about a score, and almost all show definite and more or less marked contraction of the visual fields, but no scotomata or enlargement of the blind spot.

Do these cases represent an early change in the stage of a true retrobulbar neuritis? If they do I venture to think that it throws some light upon the way in which the latter is produced, and that the optic neuritis seen in nasal sinus disease is perhaps the result of a general toxæmia rather than of direct involvement of the nerve where it lies in juxtaposition to the various sinuses.

Mr. H. M. TRAQUAIR (Edinburgh) said he had not come prepared to say anything about the investigation which had been going on in Edinburgh on this subject.

The few remarks he could make would be based upon his own experience. He had never seen any case of retrobulbar neuritis which could be traced to nasal sinus disease, in which the sinus disease was not obvious. The only cases he had seen were two or three sent by Dr. Logan Turner himself.

He thought there was a tendency to be a little vague in the diagnosis of retrobulbar neuritis, and to look upon any kind of visual defect, characterized by central scotoma unaccounted for by visible macular or nerve change, as due to retrobulbar neuritis, an actual inflammatory condition of the optic nerve being thereby signified. He thought it was necessary to distinguish pressure conditions, for example, from inflammatory conditions. Visual defects due to pituitary and other tumours were sometimes confused with those of retrobulbar neuritis. It was necessary to have regard not only to the visual symptoms, but to the complete clinical picture, and study the case as a whole before arriving at the decision that the patient was suffering from retrobulbar neuritis in the sense of an inflammatory condition of the optic nerve.

Practically all the cases he had seen recovered, and it was found, in Edinburgh at any rate, that cases of bilateral optic atrophy with blindness due to retrobulbar neuritis were quite uncommon, though unilateral optic atrophy occurred much less rarely. When the disease was bilateral the tendency to recovery was less than when it was unilateral, and this was especially so in older patients; here, again, the importance of regarding the whole clinical picture was evident. The age-incidence must be taken into consideration in deciding as to the cause of the disease and to enable cases to be classified into groups.

He did not think one could fix on any particular change in the fields of vision as indicative of retrobulbar neuritis due to sinus disease; but if the onset and course of the field changes were considered in conjunction with the general clinical conditions, a classification might be evolved which would help to place diagnosis on a firmer basis than was the case at present.

With regard to contraction of the field of vision, when the central vision was normal and the disc showed no sign of atrophy, very great caution must be exercised in coming to a conclusion. In his own view many of these cases were really functional. A similar condition had been referred to in association with pregnancy, and he thought the so-called bitemporal contraction in pregnancy was also functional. A point in distinction of functional contraction was that these patients did not complain of orientation difficulty, and here again the importance of the general clinical picture came in. A patient whose field of vision was reduced down to about 10° had the greatest difficulty in walking about and picking up small articles. It was only necessary to observe the conditions present in, for example, a case of quinine amblyopia, in which the visual field was greatly restricted to see how very important to the patient was the loss of paracentral and peripheral vision.

Another point which had been brought forward—but not at this discussion—was that the limitation of the field of vision existed for even large objects; one's hand, for instance, was not noticed until it came within the point where the field started. In diseased conditions the field of vision, in most cases, sloped gradually, more or less, to the periphery, and larger objects were observed at a greater distance out than were smaller objects. The opinion he desired to express was that, when the disc was normal and central vision was good and the patient had no orientation difficulty, one must be cautious about ascribing the contraction of the fields to organic disease of the optic nerve.

He would like to raise one point about the post-operative results in retrobulbar neuritis, namely, that it was possible the blood-letting might have something to do with the result, which was sometimes dramatic.

He would mention one case that was still under his care. It was that of a lady, aged 55, who had an attack of retrobulbar neuritis a year ago, in the right eye. In a few weeks it almost entirely disappeared. Six weeks later, however, a second attack occurred in the same eye, and that resulted in blindness and optic atrophy. That sequence of events was uncommon. A year later she had an attack of retrobulbar neuritis in the other eye, and from that she recovered. Two months afterwards there was a second attack in that eye, and this time he felt obliged, for the sake of the patient and her relatives, to recommend that some action be taken. This was agreed to, and the sinuses on that side were opened. Nothing pathological was found, but a few days after the operation the vision began to improve a little, and was now somewhat better than when it was at its worst. In that case there was no demonstrable central scotoma at that time; the visual loss was due to a general depression of the field, which diminished the acuity of vision all over.

In his experience the prognosis in these cases was worse; where there was a definite paracentral or central scotoma the prognosis was better, especially in a young woman. Was the improvement in the last case mentioned to be attributed to the operation? He did not know. Nothing was found in the sphenoidal sinus, and he did not think bacteriological examination was undertaken.

The only other case of bilateral retrobulbar neuritis he could remember which eventuated in double optic atrophy and blindness was that of a patient who, five years afterwards, was in a lunatic asylum on account of some general nervous disease.

Dr. JOBSON HORNE said there were three points to be emphasized. First, the nasal conditions and the orbital conditions which had been described might be, when they co-existed, entirely independent.

Secondly, cases were known to have occurred of blindness having followed operations upon the sphenoidal sinus and posterior ethmoidal cell.

Thirdly, in a large number of cases the ocular symptoms cleared up after simple nasal treatment such as the blood-letting and drainage consequent upon resection of the middle turbinated body.

Due observance of those three points, he considered, would guide and guard one in the diagnosis and treatment of the disease under consideration.

Mr. GRAY CLEGG (Manchester) remarked that he was also able to say that in no case of retrobulbar neuritis had he been satisfied that the condition was due to disease of the posterior ethmoidal or sphenoidal sinus.

With regard to operation, a friend of his had stated that he used to cure these cases of retrobulbar neuritis by removing the turbinates; he now cured them by leaving them alone operatively. After recovery, the appearance of the disc varied very much, and he had recorded a case in which the discs were the whitest possible, with perfect central vision and almost perfect colour fields.

Mr. A. L. WHITEHEAD (Leeds) said that this discussion was of the greatest interest to him, as some years ago he was associated with a large clinic in which he had opportunities of doing considerable nose and eye work together. His experience was much the same as that stated by some others. He had only had two cases in which optic neuritis of the papilloedema type with retinal changes was definitely connected with nasal sinus suppuration. In both these cases there existed gross disease involving the cells of the sphenoidal sinus, with a large amount of pus. After opening and draining the posterior ethmoidal cells and the sphenoid, there was considerable improvement in the vision, further improvement being prevented by atrophic changes in the retina.

With regard to the retrobulbar cases, the conclusions he arrived at some time ago accorded with those now given by Dr. Logan Turner and Mr. Foster Moore, namely, that he was unable to satisfy himself that in any case the sinus suppuration was connected with the retrobulbar neuritis by direct continuity, i.e., that there was a direct spread of infection between them. In the cases recorded that evening by Mr. Mayou, Dr. Logan Turner and Mr. E. D. D. Davis he thought there was as much probability that they were due to toxic infection spreading by way of the blood or lymph as by direct infection. Mr. Mayou quoted two cases in which no good result had followed operation, and three cases of septic disease of the antrum in which good results followed antral exploration. Mr. Davis mentioned seven cases of apparently toxic infection—from septic teeth in five—in which there was disease of antrum and ethmoid, i.e., in which there was no direct infection, but a toxic invasion from the blood. In no case mentioned was there a record of the infecting organisms. The question of sex and age was an important one in these cases. His experience of these retrobulbar cases was that in the cases in males over 40 to 50 years of age one could almost always postulate tobacco or alcohol amblyopia; and that the younger patients—mostly females between the ages of 17 and 30—almost invariably got well. In some of the cases one could trace infection in nose or teeth, and in some of the older patients he agreed with Mr. Traquair that by removing the middle turbinate—or, in the influenzal cases, by draining the posterior ethmoidal sinuses after removal of the middle turbinate—striking, sometimes dramatic, results were obtained. But those were also cases of blood infection, not of direct spread of infection to the optical apparatus.

**Sections of Surgery, Medicine, Electro-Therapeutics
and Therapeutics.**

[March 3, 1926.]

Chairman—Dr. GEORGE GRAHAM (President of the Section of
Therapeutics and Pharmacology).

**DISCUSSION ON THE TREATMENT OF EXOPHTHALMIC
GOITRE.**

IODINE THERAPY OF EXOPHTHALMIC GOITRE.

Dr. EDWARD MELLANBY, F.R.S.

[Summary.]

IT is a matter worthy of comment that in the last discussion on exophthalmic goitre, held by this Society in 1921,¹ the possibility of using iodine in the treatment of the disease was not mentioned by any of the speakers. This is an indication of the general attitude towards iodine therapy in hyperthyroidism, the usual teaching being that, although it may do good in certain cases, it does so much harm in others as to warrant condemnation. Why it should be beneficial in some cases and harmful in others was not considered.

To develop a satisfactory method of treatment of a metabolic disease along scientific lines is practically impossible so long as nothing is known as to the aetiology of the disease and but little of the physiology of the organ affected. This is the difficulty in the case of exophthalmic goitre. There is, however, one fact upon which there is general agreement which must receive consideration in any effort to evolve a method of treatment of this disease. I refer to the condition or conditions of hyperplasia of the thyroid gland found in hyperthyroidism, and the association of this with a diminished amount of iodine as compared with normal gland tissue. Marine² has also demonstrated that hyperplasia of thyroid unaccompanied by hyperthyroidism in dogs and other animals can be converted back to the normal colloid-containing structure in the course of a few weeks by giving iodine. Iodine therapy would appear, therefore, to have a strong claim for consideration in the treatment of exophthalmic goitre. This claim is strengthened by some of the remarkable effects of iodine medication in this disease.

The action of iodine in hyperthyroidism, although observed casually by earlier workers, including Trousseau, was described by Weisser³ in 1920, his observations being corroborated and extended in 1921 by Loewy and Zondek.⁴ Their work was unknown to me when in March, 1921, I described the effect of a diet containing additional iodine on hyperthyroidism before the Physiological Society (*Journ. Physiol. Proc.*, 1921), and in May, 1921, the specific effect of iodine on this condition before the Association of Physicians at Birmingham, and in the Oliver-Sharpey lectures in May, 1922.⁵ Further work on the same subject has been described by Plummer and Boothby,⁶ Starr, Walcott, Segall and Means,⁷ Cowell and Mellanby,⁸ and Fraser.⁹

¹ "Discussion on the Medical and Surgical Treatment of Graves' Disease," *Proceedings*, 1921, xiv (Clin. Sect., with Sects. Med. and Surg.), pp. 1-62.

² *Archiv. Inter. Med.*, 1909, iv, p. 253.

³ *Berl. klin. Wochenschr.*, 1920, lviii, p. 461.

⁴ *Deutsche med. Wochenschr.*, 1921, xlvii, p. 1387.

⁵ *Brit. Med. Journ.*, 1922, i, p. 832.

⁶ *Journ. Iowa Med. Soc.*, 1924, xii, p. 66.

⁷ *Archiv. Inter. Med.*, 1924, xxxiv, p. 355.

⁸ *Quart. Journ. Med.*, 1924, p. 18.

⁹ *Brit. Med. Journ.*, 1925, i, p. 1.

Small doses of iodine in the form of potassium iodide (1 gr. up to 9 gr. daily), or liquor iodi compositus U.S.P. (Lugol's solution, 15 minims), produce in most cases of hyperthyroidism a remarkable improvement in the course of a few days. The basal metabolic rate is lowered, the pulse-rate becomes slower, sweating diminishes, tremors are lessened and, in fact, all the symptoms of hyperthyroidism are profoundly influenced. This improvement is at a maximum during the tenth to the twentieth day after the beginning of iodide administration, and is then frequently followed by a gradual return of the symptoms, but these do not as a rule attain their former severity.

Iodine therapy in hyperthyroidism may result in an exacerbation of symptoms under certain conditions.

(1) In certain cases, and more particularly in those with large, hard glands, a sudden increase of symptoms may develop during the treatment. These subside after a few days, but may recur at intervals in these particular patients.

(2) If iodine treatment is stopped, more especially during the earlier months, there will be an increase in symptoms. Even after nine months of iodine therapy, ceasing to give iodine in one case brought about within a week a return of tachycardia, an increase in the basal metabolic rate and a loss of weight.

Iodine produces changes in the hyperplasia of the thyroids of these patients parallel to its influence on the hyperthyroidism. Rienhoff¹ has confirmed the earlier results of Marine and Lenhart,² and has shown that in the course of three weeks iodine brings about involution of the thyroid glands towards normal. There is an increase in size of the gland, a decrease in vascularity, an increase in the colloid, a change in shape of the acini to the round even type, and a transition of the high columnar-shaped epithelial cells to flat cuboidal and low columnar shape. So long as symptoms of hyperthyroidism are evident, iodine does not, in my experience, convert the gland completely back to normal. In two cases, even after iodine treatment had continued nine and fifteen months respectively, although the thyroid glands contained much colloid and in some parts were normal, there was still an excessive amount of hyperplasia. In both cases, also, there were symptoms of hyperthyroidism. It seems to me then, that, although iodine tends to convert hyperplasia of the thyroid associated with hyperthyroidism back to the normal structure, it does not succeed in doing this with the ease with which it carries out this process in cases of hyperplasia unassociated with hyperthyroidism. The reason for this failure may lie in some anatomical abnormality in the thyroid itself, or because there is a constant withdrawal of iodine or iodine-complex from the gland in order to satisfy some new and unknown physiological demand.

Before describing the results of iodine therapy in hyperthyroidism, apart from the immediate effects mentioned above, it may be well to state that my patients are also given a diet which, while complete physiologically so far as is known, is of relatively small caloric value.³ The reason for this is that we have found in animal experiments that, other things being equal, large energy-containing diets, which many patients with hyperthyroidism instinctively desire, tend to make the thyroids larger and more hyperplastic. It is obviously desirable to make all the conditions, so far as we know them, compatible with smaller and more normal glands.

We have now treated, at the Royal Infirmary, Sheffield, a series of cases of exophthalmic goitre and hyperthyroidism over a long period, in some instances for as long as four years. Obviously it is difficult in treating patients in an out-patient department during a period of several years to control the conditions and to collect and evaluate the results.

Apart from the advantages offered by iodine therapy in increasing the safety of surgical operations on the thyroid—a point which will be discussed by others—the

¹ *Bull. Johns Hopkins*, 1925, xxxvii, p. 285.

² *Arch. Intern. Med.*, 1911, viii, p. 316.

³ *Quart. Journ. Med.*, 1924, p. 18.

following statements represent in a general way my own experience of this form of treatment:—

(1) Most cases of hyperthyroidism are greatly improved during the first three weeks of iodine treatment. After this time, although the symptoms increase, they do not, as a rule, attain the intensity found before treatment; the patient's condition is, in fact, usually better.

(2) After two years or more of this treatment, the time seeming to vary with the previous duration of the disease and the hardness and size of the thyroid, there is generally a still greater improvement in the condition of these patients. Many of them can live normal lives, carry on their ordinary work, and can be regarded as cured.

(3) Iodine therapy in hyperthyroidism has its drawbacks and dangers, some of which have been indicated above. It is questionable whether, with our present limited knowledge of the subject, iodine therapy, apart from its use as an aid to surgery of the gland, should be practised on those suffering from hyperthyroidism with large, hard thyroids. These cases may show severe exacerbations of hyperthyroidism during treatment, and may develop difficulty in breathing owing to pressure of the enlarged gland on the trachea.

(4) Experimental work and clinical results suggest that the use of iodine in some form is an essential part of what will ultimately develop into a satisfactory medical method of treating exophthalmic goitre.

Dr. J. W. McNEE

said that his interest in the subject was first aroused in 1924, when Professor Means, of Boston, was in London and spoke enthusiastically of the effects of Lugol's iodine solution in small doses in cases of Graves' disease which were being prepared for operation. As a result of observations made since then he was certain that, within definite limitations, the revival of the treatment of exophthalmic goitre by iodine must be regarded as a great improvement. The correct time for operating on patients after iodine treatment was now well recognized, being commonly about ten to twelve days after the commencement of treatment. The optimum time could as a rule be well enough gauged by watching the pulse-rate, and without the determination of the basal metabolism. It had been said that equal improvement could be obtained simply by rest in bed. This, he felt certain, was not correct; and after the maximum improvement possible was obtained by rest, administration of iodine led to still greater fall in the pulse-rate. This point had been well demonstrated in Professor Mellanby's charts.

As a result of iodine treatment he believed the risk of operation was influenced in two ways. The general mortality rate had been definitely reduced, and surgeons could now remove with far greater safety a larger part of the enlarged gland than was generally done before the re-introduction of iodine therapy. The latter point was of considerable importance, and he had been struck with the frequency of recurrence in cases of Graves' disease in which one lobe only had been removed. In the last few months he had seen four of these recurrences, all of them operated upon before iodine had been re-introduced. In all of these patients the remaining lobe had greatly enlarged, and all the symptoms and signs of exophthalmic goitre had returned. Two of these patients had now been operated on again, after preliminary iodine treatment, with complete success.

He agreed with Professor Mellanby that although the optimum period for operation seemed to lie roughly between the tenth and fourteenth day after beginning treatment, the patients' symptoms were never so severe subsequently, even although the pulse-rate rose while iodine was being continued. Some of his (Dr. McNee's) surgical colleagues told him that they still felt safe in operating on patients under

iodine treatment even after the optimum time had passed, and the pulse-rate had begun to rise again.

An important point concerned the effects of iodine in controlling the so-called "crises" of exophthalmic goitre. He (Dr. McNee) said he had not seen in this country crises of such severity as those shown to him during a visit to the Mayo Clinic in America. It was well known, even in America, that "Mississippi valley goitre" was of unusual severity. He had seen one patient with the eyes lying out on the cheeks and both eyeballs filled with pus: this patient was acutely insane. In England such severe crises were fortunately not seen, but serious mental disturbance was by no means infrequent. What was the effect of iodine in these crises? Plummer, at the Mayo Clinic, gave large doses of Lugol's iodine, as much as 60 minims at a single dose, and to the patient with panophthalmitis two doses of 60 minims were given within twelve hours. The results in this case were astonishing, and on the following day the patient was quiet and rational. In the milder crises seen in England doses of 15 minims of Lugol's iodine have had a striking effect in controlling crises. The main point was that in such circumstances an increased dosage of iodine was essential.

Another important matter was the treatment of cardiac failure, often associated with auricular fibrillation, in Graves' disease. Plummer treated these cases with iodine, and not with digitalis, when preparing them for operation. He (Dr. McNee) had tried iodine alone in two cases of this kind, one with auricular fibrillation and large serous effusions. Iodine, even in increased dosage, was without effect, whereas on changing to digitalis the signs of cardiac failure cleared up readily enough. He hoped others might have more information bearing on this point.

Dr. McNee said he had not had the opportunity of keeping cases of exophthalmic goitre on iodine treatment for long periods, as had been done by Professor Mellanby. In the out-patients' department, however, he had continued iodine treatment for periods of several months, but he was not impressed by the results. Two of these patients had already been admitted for operation to shorten their period of illness and loss of work. He could therefore give no opinion of the value of iodine therapy when continued as the main treatment for a period of two or three years.

Dr. GUSTAVE MONOD (Vichy).

I will briefly record the following case, and leave the problem it raises to be solved by those present.

A female patient, aged 45, was admitted to hospital in Paris with a most definite complex of Graves' disease, tachycardia, enlargement of the gland, very marked exophthalmos, and fine tremor of the limbs. The basal metabolism was increased.

The patient was being submitted to X-ray treatment with no result when she developed glycosuria. The onset of this new symptom induced us to administer insulin in large doses, 40 units twice a day, on a normal diet.

As might be expected, the diabetic symptoms cleared up immediately; but the surprising feature was the very rapid improvement in all the exophthalmic goitre symptoms. As a matter of fact, beginning with the exophthalmos, every symptom disappeared, and we regarded the case as a perfect cure. Unfortunately, the patient, after a few months of normal health, developed pneumonia, and from this she died.

Cases of exophthalmic goitre are highly tolerant of insulin. It has been stated that if a dog, deprived of its pancreas, is thyroidectomized, glycosuria disappears. Now this is exactly the reverse. The law of reversibility seems to be a general law in biology, and we may wonder whether, just as thyroidectomy causes a marked increase in the amount of islet tissue in the pancreas, so, reversely, when we supply insulin to the body, do we not act in the same way as if we were performing thyroidectomy?

Professor FRANCIS R. FRASER, M.D.

During the last five years fifty cases of exophthalmic goitre have been treated with iodine in the wards of the Medical Unit at St. Bartholomew's Hospital. We have used the 10 per cent. solution in 95 per cent. alcohol, and have selected this preparation because it contains no combined iodine, such as iodide. It is now known that any form of iodine that is ionized acts as well as any other. Lugol's solution is used largely in America. It is richer in iodine than the 10 per cent. solution, and the *tinctura iodi mitis* (B.P.) is poorer, so that, when prescribing, care must be taken to ensure that the desired dose of iodine is administered. At the commencement of the work the correct dose was not known, and in some cases too much was given and more harm than good resulted. As much as 180 minims a day were given in some cases, and although an immediate remission of the symptoms, a fall in the basal metabolic rate, a fall in the pulse-rate and a rise in the body-weight occurred, as has been described by Professor Mellanby, deleterious effects were seen later. These were of two types. In some, symptoms of iodism, i.e., running at the eyes and nose, resulted, but in others an enlargement and hardening of the thyroid gland was produced, together with tachycardia, palpitations, and a sensation of choking. From these early experiences the dosage now used was evolved.

The patients are kept in bed for one to two weeks in order to estimate the severity of the intoxication and the basal metabolic rate. They are then given 5 minims of the 10 per cent. solution three times a day—a total daily dose of $1\frac{1}{2}$ grains. When the maximum improvement is obtained, the dose is reduced to 10 minims a day, and before the patient leaves hospital it is reduced to 5 minims a day. No patient is sent out of hospital on a larger dose than this. If on larger doses than this for a long period of time, and in the absence of skilled observation, there is danger of harm and of increased intoxication. Even when under observation harm may result with these smaller doses in the cases of secondary Graves' disease. These are the cases that have had a simple goitre for perhaps years previous to the appearance of symptoms of intoxication, or that have a hard knobby goitre, or a small fibrotic thyroid gland. Not only do these cases not stand the larger doses of iodine so well as the cases of primary Graves' disease, but the dramatic improvement is not so often seen in them. In them the smaller doses must be used, and many cannot take more than 2 minims a day. By carefully adjusting the dose it is probable that every case with symptoms of intoxication can be benefited; the correct dose must be found for each case.

Dr. McNee mentioned that cases with circulatory failure do not respond well to iodine. Since these cases are usually examples of secondary Graves' disease, this is to be expected. Prof. Mellanby has spoken of the value of long-continued administration. We have had cases that have taken iodine for four years, with occasional short periods without it. When it is stopped, these patients ask to be put back on iodine, and I am convinced that they feel better when on it.

The value of iodine in the treatment of exophthalmic goitre consists in the fact that by careful adjustment of dosage the general level of intoxication at which cases run their course is lowered and that by its use surgical treatment is made safer. If a patient is going to recover spontaneously, by lowering the level of intoxication the period of incapacity for work is shortened and the danger of severe exacerbations and cardiac failure is lessened. In many cases there are patients who would be permanent invalids if surgical treatment were not employed, and iodine is used so that they may be at the lowest level of intoxication possible at the time of operation. After operation, cases seem to improve much faster when iodine is recommenced, so that it is advisable to continue the administration throughout convalescence, perhaps for several months.

(Lantern slides illustrative of the effect of iodine were shown.)

These cases illustrate the fact that the iodine effect is not permanent. On stopping the administration the condition will relapse, and a second administration will be less effective than the first. Even when the patients are on iodine relapses occur because of tonsillitis and excitement and emotion, such as is caused by trouble at home or anxiety to get back to the children. The last slide shown exhibits an unusually marked effect in lowering the pulse-rate in a fatal case of exophthalmic goitre complicated by streptococcal septicæmia.

It is to be hoped that nothing will be said in this discussion likely to make it appear that iodine therapy in exophthalmic goitre is a simple treatment to carry out effectively. Much harm is being done by such statements. If iodine is used, the patient must at first be under daily observation, preferably in bed. If a patient under iodine treatment is allowed to pass out of observation, this must not take place until the case has been thoroughly studied and the response to the dose employed known.

Dr. J. A. RYLE

said that it had been suggested to him that he should state the opinions of those opposed to the employment of iodine. He had not, however, had enough experience of the treatment to speak critically. He could only be said to oppose it in so far as he was an opponent of over-zealous attempts to find a specific method of therapy for what was so obviously a non-specific disease. The recent tendency had been to seek for a biochemical answer to the therapeutic problems of exophthalmic goitre and also, in his opinion, to lay too much stress on the importance of surgical or purely physical methods of treatment. Perhaps he could suggest a line of critical thought in regard to the problem. It was notoriously difficult to draw conclusions about the results of all therapeutic experiments. Even when taking a disease due to specific agents, such as typhoid fever or pneumonia, it had been found impossible to produce reliable evidence as to the value of any particular line of specific treatment. In a non-specific disease like exophthalmic goitre it was even more difficult to draw conclusions. There was little accurate knowledge as to the causal pathology of the disease; it was generally presumed that several factors were at work. There might in any case be contributory factors of a physical, chemical or infective kind, but in almost every case there was a strong emotional factor underlying both the initiation and perpetuation of the symptoms. If the emotional factor was regarded as predominant, extreme caution was necessary, not only in deciding upon the employment of purely physical or chemical lines of treatment, but still more in assessing their results. No one would deny that iodine produced a definite effect in certain cases of exophthalmic goitre, but that was a different thing from saying that it influenced the later course of the disease. Salicylates exerted a definite physical effect upon rheumatic fever; most, however, would dispute that salicylates had any definite effect on its subsequent pathological course. Before pronouncing judgment on any therapeutic problem one essential preliminary was a familiarity with the natural history of the disease when left to itself and under varying conditions.

Sir William Hale-White showed in the Guy's Hospital reports (1911),¹ and in the course of a discussion before this Society² a few years ago, how necessary it was to be acquainted with the disease when left to itself. He showed that there was a clear tendency to spontaneous recovery, and also that the prognosis of the disease in private practice and in hospital was very different. In hospital the prognosis seemed sometimes to depend on the particular ward the patient happened to be in. His (the speaker's) own impression was that when the physician was optimistic and reassuring, and left his cases alone, he obtained better results than the zealous, scientific physician who investigated with energy, and, perhaps pessimistically, discussed surgical aspects.

¹ *Guy's Hosp. Rep.*, 1911, lxx, pp. 1-32.

² *Proc. Roy. Soc. Med.*, 1921, xiv (Sects. Clin., Med., Surg.), p. 14.

A paper which had not attracted the attention it deserved in this country was that of Kessel, Lieb and Hyman (*Archives of Internal Medicine*, 1923), which dealt with fifty cases of exophthalmic goitre, all in wage-earners, and all fully investigated from every standpoint. They were treated by the method of "skilful neglect," were placed in good surroundings, under a cheerful sister, and, apart from the removal of obvious focal sepsis, there was no special treatment. The fifty cases were followed up for two years, and at the end of that time forty-one (82 per cent.) had returned to their ordinary life and work, and were regarded as socially and economically restored. These results compared favourably with those from any other method of treatment. Of the cases which died, three were from causes other than goitre. With appropriate physical and psychological handling in the early stages it should rarely become necessary to call upon the surgeon for aid. The psychological aspects of the disease were still receiving inadequate attention. There was, he thought, a certain danger in broadcasting observations about such ultra-specific methods of treatment as iodine therapy and thyroidectomy, for there was a natural tendency in the profession, particularly in the case of difficult and obscure diseases, to grasp, not always judiciously, at any treatment which had a specific sound about it. It was clearly established that iodine was a help to the surgery of exophthalmic goitre, but it was of more limited value, in his view, as an aid to medical treatment. On the whole, he would rather treat a case with optimism than with iodine.

[March 9, 1926.]

Chairman—Sir G. LENTHAL CHEATLE, K.C.B., C.V.O., F.R.C.S.
(President of the Section of Surgery.)

Professor FRANCIS R. FRASER, M.D.
(From the Medical Professorial Unit, St. Bartholomew's Hospital.)

General Management of Exophthalmic Goitre.

THE general management of cases of exophthalmic goitre is so wide a subject that it is not possible in the time allowed to refer, however briefly, to many important methods of treatment. The cause of the disease is unknown, and so no treatment directed at the cause is possible. Recent developments have, however, made it advisable to review the situation in order to improve the general management in the light of these developments. They are: (a) The re-introduction of treatment by iodine; (b) the recognition of thyroid disease as a cause of auricular fibrillation and heart failure; (c) improved skill in the surgery of the thyroid gland and in the selection and preparation of patients for operation.

CLASSIFICATION.

It is unfortunately necessary to discuss briefly what is meant by the term "exophthalmic goitre." If we exclude cases of cretinism and myxœdema, and cases of simple goitre in which there are no symptoms other than those of an enlarged thyroid gland, or such as are the mechanical results of the enlarged gland, and omit cases of thyroiditis and of malignant disease, there remains a large group of cases of goitre with symptoms of thyroid intoxication. The term "hyperthyroidism" is frequently used in the same sense as "thyroid intoxication" is used here, but, for various reasons which cannot be discussed here, the term "hyperthyroidism" is unsatisfactory and is being gradually replaced. Among the cases with symptoms of intoxication there are those with diffusely enlarged, very vascular goitres, and the classical picture of Graves' disease with its eye signs, tremor, tachycardia, and peculiar, excitable, nervous and mental state. There are other patients in whom the

symptoms of intoxication appear after perhaps years, during which a simple goitre has been present. In these cases the general intoxication is usually less, the eye signs are slight, but the cardiac disturbance is relatively more prominent. This same clinical picture is seen in a larger group of cases that have no previous history of simple goitre, but in whom the enlargement of the gland is irregular, or the gland less vascular and harder than in the typical form, or scarcely enlarged at all. In the first group histological examination usually shows a change involving the whole gland, which suggests great activity of the secreting cells and an absence of colloid storage. In the other groups areas of similar activity are seen, but they are localized, colloid storage is present, and, in addition, there is a fine or a coarse fibrosis. The fibrosis may be so coarse as to give the appearance of multiple adenomata, and various forms of degeneration may be present in localized areas. In the present state of our knowledge, I propose to use the terms suggested by Williamson and Pearse [1] and call the first group of cases "Primary Graves' Disease," and the others "Secondary Graves' Disease." Their terms are based on histological examination, and although it is clinically possible to recognize many cases as belonging to the primary group and many as belonging to the secondary group, there are many that are difficult to place, on clinical evidence alone. I find it difficult to recognize a clear distinction between those with eye signs and those without, and therefore at present include the cases described by Plummer [2] as "toxic adenoma" in the secondary group, which includes also "toxic adenomatosis," "toxic goitre," "incomplete" forms, "*formes frustes*," "thyrotoxicosis," &c. Without doubt further work and experience will allow of more exact differentiation, but this distinction between the primary and the secondary groups has some importance in treatment and prognosis.

(Lantern slides were shown illustrating the pathology.)

ETIOLOGY.

We are quite ignorant of the cause of primary Graves' disease and quite ignorant of the cause of the onset of symptoms of intoxication in secondary Graves' disease, but in both forms of the disease exacerbations and relapses are common features, and there are certain factors associated with these. Adolescence, pregnancy, the puerperium and the menopause appear to be dangerous events, and may be associated with increased intoxication. Infections, and above all, septic tonsils, nasal sinuses and teeth sockets are particularly important because so often overlooked, and are frequently responsible not only for exacerbations and relapses but also for maintaining a high level of thyroid intoxication. Worries, mental stress and shocks are also important and are frequently acknowledged by the patients, but are sometimes not disclosed until inquired for.

COURSE OF THE DISEASE.

Before one can consider the measures to be employed in management, it is necessary to have as clear a knowledge as possible of the natural course of the disease. This knowledge is difficult to obtain, since hospital records deal with the more severe cases only, and social position enters greatly into the possibilities of adequate management. Barker [3] has stated that the course of the disease associated with diffuse hyperplasia of the whole gland, that is, primary Graves' disease, "is probably two or three years, no matter how you treat it (medically, surgically, radiologically)." He mentions, however, that relapses occur. Kessel, Lieb and Hyman [4] studied fifty cases, and maintained that recovery sufficient to enable a resumption of work resulted from rest and symptomatic treatment only, without surgical or X-ray treatment. Read [5] published composite curves to show that the progress as measured by the basal metabolic rate is much the same, no matter whether general medical measures, X-rays or surgery are employed. Holmes, Means, Porter, Richardson and Starr [6] confirm this in general, but show that treatment by subtotal

thyroidectomy has a definite effect on the course. My experience is, generally, in agreement with these views, but the frequency of relapses robs the main contention of much of its significance.

In secondary Graves' disease, although the general level of intoxication is not so high, the tendency to recovery is not so great. The condition is much more chronic, and after years of exacerbations and remissions cardiac disturbances, auricular fibrillation, heart failure, mental disorders and increasing emaciation not infrequently develop, and may so dominate the picture that the causal condition is not always recognized. The basal metabolic rates seldom rise to the heights seen in the primary form. I suspect that a case showing the features of primary Graves' disease in early life may later present the clinical and pathological features of the secondary form, but there is at present a lack of dependable records of the life histories of these cases, and the ultimate results are still quite unknown.

MANAGEMENT OF PRIMARY GRAVES' DISEASE.

Even if there is a tendency towards spontaneous recovery in primary Graves' disease, cases may flare up and the patients die with severe intoxication. What is perhaps of greater importance is that during the period of months or years in which the disease is running its course the patients are often quite unable to carry on their work. It is necessary that they should be managed so that the level of intoxication at which the disease runs its course should be as low as possible.

Rest.—Of all the methods of treatment rest is the most important. The patient should be put to bed and observed for a week or more without any other form of treatment, so that the severity of the condition may be estimated. Physical rest is not more important than mental rest. Whether the rest should be given in hospital, at home, or in a nursing home, must be a matter for careful consideration in each case. Temperaments, not only of the patient, but also of the relatives, must be considered. The financial status is most important. The usual daily duties must be known. After the first few weeks the rest need not be absolute, for if too strict it leads to restlessness, and some employment for body and mind has a beneficial effect on both. If the heart is grossly dilated, or the general intoxication increasing, strict rest is essential. I do not think that tachycardia, or a moderately increased basal metabolic rate, is an indication for strict enforcement of rest in bed. The influence of the mind in this disease is great, and detailed attention to the surroundings and to the cheerfulness of the attendants is always necessary.

Elimination of Sepsis.—During the preliminary period of rest a thorough search for infections is made. Even if no evidence is found of tonsillar infection, a history of sore throats during the onset justifies an examination by a throat specialist. Sinuses and teeth must be examined and any suspicion of infection cleared up. In several cases that were not improving as quickly as was hoped, an onset of acute tonsillitis has unmasked buried sepsis, and such an occurrence, though it causes a distressing exacerbation, should be viewed with satisfaction, as a cause for the unsatisfactory condition has been found and can be dealt with. In sixty cases of all forms of Graves' disease that have been under the care of the Medical Unit at St. Bartholomew's Hospital in the last five years tonsillectomy was performed in fourteen, and in each case for gross sepsis. In such cases the disease runs its course at a lower level after the operation, and the danger of a serious exacerbation is greatly diminished.

Iodine.—The re-introduction of the use of iodine has been of considerable value in enabling the disease to run its course at a lower level, and in checking the severity of exacerbations, but it need not be considered in detail to-night as this subject has been discussed at a recent meeting of the Society.

Diet.—Diet must be mentioned if only to say that at present there is no clear indication of the value of any special diet. The diet must be liberal, as the patients

are often hungry, and since their general metabolism is raised it may be presumed that they require a higher caloric intake than is normal for their size and their external activities. At present an ordinary diet, arranged to suit the habits and status of the patient, is all that is indicated, but it must be liberal.

Many other methods of treatment, by drugs, by hydrotherapy, by physiotherapy, &c., have been used, but I believe that they are all either symptomatic or exploded, and it would but cloud the main issue to discuss them, however important, as symptomatic treatment, they may be. Of treatment by X-rays and by insulin I have practically no experience and will not discuss them, but doubtless others will consider them fully to-night.

RESULTS AND INDICATIONS FOR SURGICAL TREATMENT.

If treatment is carried out on the lines I have mentioned, most of the cases of primary Graves' disease make a satisfactory recovery and the patients return to nearly normal conditions of life and efficiency. Many, perhaps, do not require even as much treatment as I have suggested, but these we are not in a position to study in hospital practice. Of the patients that attend hospital, many are quite unable to carry out such treatment. The absence from heavy household duties or from business worries, which is so essential, results in other worries, or in financial straits, that rob the rest of all value. Such patients must be returned to their ordinary duties within a relatively short period of time. By surgery this can be effected.

If, under good conditions, a satisfactory improvement has not been effected in six months, so that a return to work can be at least attempted, operation should be considered. If at the end of six months the pulse-rate at rest remains constantly above 100, or if serious cardiac disorders such as auricular fibrillation develop, operation should be considered. Of the thirty-two cases of primary Graves' disease that have been in the wards under my direction in the last five years fourteen have required operation: one only for persisting general intoxication, three because of auricular fibrillation and heart failure, and ten on economic grounds. Of the eighteen patients who did not undergo operations, eight are doing well, three improving very slowly, two are doing badly and are practically confined to bed, three are dead, and two lost sight of. Of the fourteen that have had operations, one died immediately afterwards, and I feel sure that with our greater experience now in the preparation of the patient and the selection of the optimum time this death could have been avoided. The other thirteen are all doing their work successfully, but still show signs of the disease, and at times of stress recognize that their capacity for work is limited.

MANAGEMENT OF SECONDARY GRAVES' DISEASE.

The general management of cases of secondary Graves' disease is on similar lines. The degree of general intoxication is usually less, and many cases can be guided through life with little interference with their activities. The effect of iodine is generally less marked, and great care must be taken not to do harm rather than good by its use. The more chronic course and the absence of the tendency to spontaneous recovery render these cases more serious in their prognosis, especially as cardiac disturbances and congestive heart failure are their prominent features. In them, therefore, surgical treatment is more clearly indicated once a serious degree of crippling is reached. A few years ago the cases of auricular fibrillation and oedema would have been considered impossible cases for successful operation, but under the improvement in surgical skill, and the more efficient selection and preparation for operation, these are the cases in which the indication for surgical treatment is most clear (Dunhill, Fraser and Stott) [7] and in which the results are most striking. Of twenty-three cases of secondary Graves' disease, ten patients were treated on general lines, and of these five are continuing satisfactorily, one is doing badly and has now developed auricular fibrillation, one has been lost sight of, and three died before they

could be brought to a satisfactory state for operation. The remaining thirteen patients have undergone thyroidectomy operations. One of them has recently died in hospital when re-admitted for further thyroidectomy two years after a lobectomy, and the other twelve are doing well. Seven of them had auricular fibrillation and heart failure and are all now free of cardiac irregularity. In preparing these cases for successful operation careful treatment with digitalis is necessary, and much patience on the part of the physician is required. While in some the auricular fibrillation disappeared spontaneously after operation, in others the administration of quinidine was necessary to effect a return to normal rhythm.

In considering the high proportion of operated cases in our series, it must be remembered that we only see in hospital the cases that are doing badly or that are not improving satisfactorily relative to their financial position or the necessity for an early return to work. That these patients can be saved from death or invalidism, or restored to economic efficiency, is dependent on the co-operation of a skilled and experienced surgeon, but both the physician and the surgeon must guide continually for long periods both before and after surgical treatment to obtain the maximum beneficial results.

REFERENCES.

[1] WILLIAMSON and PEARSE, *Journ. Path. and Bact.*, 1925, xxviii, p. 361. [2] PLUMMER, *Mayo Clinic Papers*, 1913, v, p. 447. [3] BARKER, *Internat. Clinics*, 1924, i, p. 1. [4] KESSEL, LIEB and HYMAN, *Arch. Int. Med.*, 1923, xxxi, p. 433. [5] READ, *Journ. Amer. Med. Assoc.*, 1924, lxxxiii, p. 1963. [6] HOLMES, MEANS, PORTER, RICHARDSON and STARR, *Boston Med. and Surg. Journ.*, 1924, xcvi, p. 295. [7] DUNHILL, FRASER and STOTT, *Quart. Journ. Med.*, 1924, xvii, p. 326.

OPERATIVE TREATMENT OF EXOPHTHALMIC GOITRE.

Mr. T. P. DUNHILL, C.M.G.

I am speaking to-night almost entirely about the operative treatment because I have been requested to do so; but I wish to make it clear in the beginning that I do not regard operation as the one and only treatment for every stage of this disease. For some stages of the disease I do regard it as the main treatment.

It is impossible to compress into a twenty minutes' address all the material which is of interest, therefore I propose to leave out much, to skim/rapidly through other aspects of the subject and to concentrate on such points as appear to be most profitable for discussion.

I have thought that what would best serve this purpose would be to speak under the following headings:—

- (1) *How cases are selected for operation.*
- (2) *How operation can be made safe and effective.*
- (3) *Death-rate and morbidity.*
- (4) *End-results.*

Every case of toxic goitre must be treated on its own merits, but if we are to discuss principles of treatment, we must have a working classification of cases. It can be simple, and must therefore be arbitrary. For other purposes we have the masterly classification of Scott Williamson and Miss Pearse [1], but the one I speak of is a simple sorting out of cases.

I divide patients into five classes:—

1st Class.—Those in the first six months of the disease. They differ in degree. In some it starts insidiously with so little obvious disturbance that the diagnosis is at first unsuspected. In some it starts much more floridly, all the signs developing early, sometimes accompanied by severe gastro-intestinal disturbance.

2nd Class.—Those who, at the end of six months, have not regained normal health but who have not yet reached the stage of heart failure. Those in whom the disease began with slight symptoms have settled into a state of chronic ill-health. Those in whom the onset was severe have also settled into a more chronic condition. The disability of patients in this class may vary within wide limits; they may carry on their work, better at times, worse at times; generally speaking they are too

ill to work. The majority of the patients who wander from hospital to hospital are in this class.

3rd Class.—Those from the previous classes who are now in a state of visceral degeneration, chiefly de-compensated hearts, as shown by established auricular fibrillation, or marked œdema or anasarca. I do not mean simply the swelling of feet or ankles. These patients are permanently invalided. In this class we must place those in whom the restlessness of the disease has caused such mental disorder that it has become practically impossible to nurse them in their own homes, and also those in whom glycosuria has developed.

4th Class. Formes Frustes.—We each have our own idea as to what the term "*formes frustes*" indicates. I do not take it to include toxic adenoma. It includes cases that are not typical; where, with some symptoms of Graves' disease such as exophthalmos, there is excessive obesity, or where, with the other symptoms characteristic, there appears to be no goitre present.

5th Class.—Cases which have been described and published by all of us, called by Plummer toxic adenoma, by others secondary Graves' disease—not really Graves' disease at all. There is a unilateral or a nodular goitre which has existed for years without giving trouble. Then cardiac signs, often of a serious grade, have developed, but the nervous phenomena are absent or only slightly developed.

Patients in this class scarcely come into our discussion to-night, and they are not included in my statistics, but they must be mentioned so that our minds may be clear as to what we are talking about.

The foregoing is an arbitrary division, but it gives a working plan upon which we can begin to discuss the question of operation.

(1) HOW DO WE VIEW THE PATIENTS IN EACH OF THESE CLASSES AS REGARDS THE ADVISABILITY OR THE NECESSITY FOR OPERATION?

Class 1.—It may be stated as a general rule that patients in the first six months of the disease do not require operation. Cases that are mild should be piloted in ways that have been sufficiently indicated to you.

There must be many people who nearly fall victims to the disease and just do not. There must be many who fall victims who could be cured, if at that early stage the causes that induced it could be removed. The very grave cases commencing with vomiting and diarrhoea require careful management in ways that have also been indicated to you; but it must rarely happen that, in either the mild or the grave case, the best interest of the patient would be served by operation. During this six months, most patients who have not been cured by medical means reach a point of maximum severity and then subside into a chronic stage. These constitute the second class.

Class 2.—It is in this stage that there will be most dispute regarding the advisability of operation. It has been stated by Barker [2] that all patients get well equally quickly whether they are treated medically, by X-rays or by operation, and that the average time taken is two or three years. Those practitioners whose experience has made them feel that this is true and whose patients can afford the time and obtain the necessary nursing, will naturally and rightly treat their patients along medical lines. But first we want to know if the statement is true. It is not my experience. From the 831 patients upon whom I have operated for exophthalmic goitre, I have made a careful analysis of the histories of 170 consecutive cases and have been able to determine fairly accurately the length of time these patients have been ill before operation was performed. (A table showing these periods is exhibited.) Another fact to be borne in mind is that all the patients in Class 3, the class with visceral degeneration, which we come to next, are examples of the failure of medical means to stay the course of the disease, so that in considering the welfare of the patients who constitute Class 2 we must take into account the morbidity and the

economic factor. This class is largely made up of women in the early middle period of life, young women who have to earn their living, and mothers of families. Therefore, in this class the social position of the patient counts for much. If the individual can afford to live a sheltered life with efficient nursing, possibly for years, well and good. The practitioner will watch the heart and mentality of the patient, and if either show signs of being affected, it will indicate that something more radical should be advised. With the poorer patient it is altogether otherwise. I find numbers of these patients coming to the out-patient department, ill, unable to work, with no place at which they can be nursed, and, with it all, having in some way others dependent on them. It seems to me essential to cut short the disease and restore the patient to an industrial plane as soon—after the first six months—as it is realized that the patient is not improving. It remains with us, as surgeons, to show that this can be done, and done with safety.

Class 3.—Patients who have drifted on through the first and second stages until the heart has given way under the continued intoxication. There is auricular fibrillation, or established cedema, or both.

In the first class operation is rarely indicated. With regard to the second class opinions may differ, but in this third class I believe medical treatment can rarely restore the heart to permanent normal rhythm and functional efficiency. This result is now being achieved by operation in a sufficient number of cases to enable it to be known that very striking benefit can be depended upon. How complete, or how permanent this will be, will be discussed later.

Class 4.—*Formes Frustes*: I do not take "*formes frustes*" to mean the toxic adenomatous condition accurately described by Plummer and generally noted by many observers long before him, but a condition in which the aspect of the patient appears to be that of Graves' disease, and in which there is some sign which appears unusual or wanting. For example, the patient, instead of being thinner than normal, is grossly fat, or notwithstanding the exophthalmos and rapid heart, there is no detectable enlargement of the thyroid gland. A clearer appreciation of the pathology of these conditions will be obtained from the work of Scott Williamson and Pearse above referred to [1].

I think we should not let these cases, which really form a very small proportion of the total number, obscure the discussion, for I take it that, to-night, we are making an attempt to obtain a clear view of the chief problem, namely, the position that operation should take in the different stages of characteristic cases of exophthalmic goitre, beginning at its inception and going on to the late stages of cardiac de-compensation; and that because operation is of great value in some stages, it should not be pushed as the treatment in every kind of thyroid dystrophy.

Class 5.—These patients may be gravely disabled by thyroid toxæmia with cedema and irregular heart action. I believe they cannot be cured by medical means. At any rate, patients are not infrequently seen who have been completely invalidated for eight or ten years under good medical guidance, and during all this time the disease has been steadily progressive. The danger of operation is not so great as in true Graves' disease, and the response to operation is prompt. These are not classed among my cases of exophthalmic goitre.

(2) HOW CAN OPERATION BE MADE SAFE AND EFFECTIVE?

I have stated the conditions for which I regard operation to be advisable. If it is helpful to some patients, you will want to be satisfied on two points: (a) *How can it be made safe?* (b) *How can it be made effective?*

Regarding (a) *How can operation be made safe?*

(1) *By ensuring that the patient has no other load to carry besides the disease itself.*—It is surprising to observe to what extent patients are still sent for operation with foci of gross sepsis present. This is very reprehensible. The majority of patients

improve obviously when septic foci are cleaned up, and in an operation where the margin of safety is narrow enough, every factor which reduces this margin should be eliminated. It should not be necessary to have to insist on this at such a late period.

(2) *Rest in bed.*—It takes several days for the pulse-rate to come down to its resting level when a patient is put to bed.

(3) *Iodine medication.*—This should be commenced as soon as it is seen to what extent the pulse-rate has dropped as the result of rest and freedom from worries—usually about the third day. Not only will iodine further reduce the pulse-rate, with the associated improvement in the patient's condition, but it will induce a definite change in the pathological state of the gland, which makes the operation safer. We do not know enough about this yet, but we believe that it sets up colloid vesiculation and possibly pressure obliteration of blood-vessels.

(4) *Confidence between patient and surgeon.*—It is not enough that confidence has been established between patient and physician. On the operation morning the surgeon must come as a friend, not as a person to be feared. This is not an emergency operation. A surgeon is not called in as he is when he operates upon a perforated gastric ulcer.

(5) *Adjusting the amount done at one operation to the patient's strength.*—This is most important, and the surgeon must be able to gauge that amount. It is always tempting to continue and get the complete job done in one operation. The patient who has been ill for a long time will often plead for the whole operation to be finished at once; and for the surgeon it is far easier to deal with the second lobe in a field unhampered by scar tissue. This is sometimes possible, and if so, it is the right thing to do; but until the surgeon can judge of this, he will tell the patient in the beginning that two operations are necessary, and then, without disappointing her, do at one stage only what is within her strength to bear.

In dealing with the third class—those with irregular dilated heart and œdema—safety is only attained by the closest co-operation between surgeon and physician. In this class the results obtained are sometimes hardly credible, but the margin of safety is very narrow. A surgeon may be able to, but can scarcely be expected to, sort out cases of flutter from those of fibrillation, and know from an electrocardiogram when heart block is present. Nor does the surgeon know just the amount of improvement in the pulse deficit that can be expected, the amount of digitalis that will achieve this, and how the dosage of this is to be planned; nor, when a patient is waterlogged, can a surgeon be expected to know how best to employ the diuretics or measure fluid intake against urine output. Therefore, in his hospital, he will associate himself with a physician who is interested in these matters, and day by day the two will work in their wards together. Without this close co-operation, patients in this class cannot be operated upon safely or the desired result attained.

If these precautions are taken, always excluding the moribund, there are few patients who cannot be carried through operation with a reasonable degree of safety; but no consideration of urgency on the part of the patient, or convenience on the part of the surgeon, should ever tempt him to operate at a time other than that which is the optimum, taking all the factors into account.

(b) *How can operation be made effective?*—There are many patients who have been operated upon for exophthalmic goitre who are not cured. Dr. McNee laid stress on this point last week. Earlier publications on operative results have been misleading.

Kocher [4] stated that removal of one lobe, with the isthmus, and ligation of an artery of the other side, cured 83 per cent. of cases. Similar statements were published by American surgeons. I had realized in 1907 [5] that this was not so. The remaining lobe is bigger than the whole normal gland and very toxic. It is not reasonable to suppose that the patient could be cured while all this remained behind.

This point must be realized at the beginning. The removal of the first lobe is comparatively easy. Removal of the appropriate amount of the second lobe is more difficult. The approach is through scar tissue, the anatomical planes may have been destroyed by adhesions, and an extremely vascular gland is to be cut through; but unless the surgeon is prepared to undertake the second, he must not do the first. Removal of one lobe improves the patient so much at first that patient and surgeon are pleased, but this result is so far short of a cure that, if left at that, it can only bring the operation into disrepute. The pulse-rate will not remain down; the eyes will not recede, and in patients with auricular fibrillation there will not be restoration to normal rhythm. To make the operation effective, sufficient gland substance must be removed to reduce the secretion to the minimum compatible with the physiological needs of the body.

(3) DEATH-RATE AND MORBIDITY.

The death-rate for this operation will vary within wide limits. It will vary according to the type of patients operated upon, and greatly according to the time selected for the operation in each individual. It will also vary according to the care with which the preliminary treatment has been carried out. Some surgeons are careful for their statistics; others will undertake operation at some risk on patients who, without operation, are, as far as can be judged, doomed to complete invalidism; lastly, it will naturally vary according to the experience of the operator.

My own death-rate in 831 operations for Graves' disease—excluding toxic adenoma—is 2.9 per cent. It became rather higher three years ago when we were feeling our way with some very severe cases, but owing to better preliminary treatment, to selection of time, and—at hospital with severe cases—to the co-operation of my medical colleague, Professor Fraser, eighty-five patients were operated upon between the last two deaths, many of these being extremely ill people.

(4) THE END-RESULTS AND ADVISABILITY OF OPERATION.

It may be asked, if the risks of operation are only to be successfully negotiated by extreme care, if a certain degree of skill and judgment are necessary and if there are other satisfactory methods of treatment available; if Dr. Barker is right when he states that patients recover in two or three years whatever the course pursued, then why operate? Well, is that statement true? I have had 170 consecutive cases analysed very carefully: I find that sixty-eight of them have been ill over four years, forty-eight over six years, thirty-seven over eight years, and thirty-two over ten years. Therefore, in time alone, wastage is very high.

Next, in what condition are these patients? I find that of these 170 patients, thirty have had a heart beating with permanently irregular rhythm. In most of these I have electro-cardiographic demonstrations of this fact. Some were far too ill to be sent for this examination to be carried out. I do not include in this number those with temporary fibrillation. Glycosuria, corneal ulcer or a severe grade of oedema had occurred in many cases. In others, the restlessness had progressed to the stage of severe mental disorder.

I have seen auricular fibrillation begin intermittently and become permanent; I have seen corneal ulceration occur and witnessed mental derangement becoming more pronounced while patients are under treatment. I am therefore compelled to believe that Dr. Barker's statement is not a true statement of the case.

I am not dealing with the question of the patients who are cured. I know as well as my medical colleagues how many are cured, and I also know that if we were living in a modern Utopia instead of a rather hard modern world, patients would not come to the condition I have described, but while we are all trying to eliminate the causes of this disease, we have to deal from time to time with a situation that is present.

End-results.—What evidence can we produce that surgical treatment will shorten the duration of the disease or restore to normal function organs which have shown evidence of failure? I have selected some photographs to illustrate different grades of the disease and the response to operative treatment in each.

(1) Two young women, whom I place in the second class, that is, they had been ill more than six months but had no heart failure. One of them was earning her living by working in the General Post Office, the other was occupied with rather difficult home duties. The first went back to her duties immediately on her return from the convalescent home and has worked continuously for four years since. She feels quite well. The second, whose exophthalmos was such that she suffered from corneal ulcers both times she was in hospital, went home to nurse an invalid father who, apart from her day work, calls her out of bed several times every night. She states that she has not felt so well for many years. A fireman on the northern express service went back to his duties after his return from convalescent home, and has carried on continuously since.

(2) The next two photographs illustrate the disappearance of exophthalmos after operation.

(3) Passing next to patients in the third class, namely, those with cardiac failure. The slides shown are those of electro-cardiograms of patients with permanent auricular fibrillation before operation and showing normal rhythm after operation. One of these patients, we believe, had fibrillated for eight years, another for five years. Leaving out of account the temporary fibrillators, I operated upon eighteen who were permanently fibrillating between 1921 and 1924, ten more during 1925 and four more this year, and of these almost all have regained normal rhythm. This is interesting in another aspect. We do not yet know the origin of this disease, but the disappearance of fibrillation after operation shows that the origin of the toxins, which cause some of the most distressing symptoms, is in the diseased thyroid gland.

(4) The next slide shows a chart illustrating the increase in the amount of urine immediately following operation in a water-logged patient in whose case diuretics had been ineffective. This patient arrived from South Africa as ill as a patient could be. Legs, thighs and trunk, as far as the epigastrium, were enormously distended: the abdomen contained fluid; she was dyspnoic, and the daily amount of urine passed was about one pint; the heart had been irregular for five years. She was kept for a month, while every effort was made to increase the excretion of the urine, decrease the dropsy and diminish her breathlessness. She was worse rather than better at the end of the month; and then one lobe was removed. You will see that in three days the output of urine rose suddenly to 60 oz. and then to 90 oz., and simultaneously the oedema disappeared. Part of the second lobe was removed later. She went back to South Africa by herself. She now camps out, rides on horseback and manages her household affairs.

MENTAL DISORDER.

One further aspect that remains to be discussed is mental disorder. This complication is not common, but, taking a large number of cases, it is not infrequent. I could give instances of patients who suddenly became worse and died.

I have had to decide what course to follow in seven cases in which the patients were gradually getting worse, and who were approaching, or had reached, a stage at which they could not be managed in their own homes. I have never operated upon these patients without the fullest consultation and without the relatives appreciating all that there was at stake. It is wise to have the help of a specialist in mental disorders before a decision is arrived at. Only one of these patients has not improved; the others have, after operation, returned to their ordinary way of living. One of them has since married, and one of the worst was driving her own car around London within eight weeks of her second operation.

The degree of recovery in these cases appears to be very high, and yet I think this is the appropriate place to say that I believe the secretion is not normal secretion, and that by reducing its amount by four-fifths we are not leaving a patient with an output of secretion normal in amount and quality and free from toxic substances; and that therefore the end-results are not comparable with those obtained after

removal of a diseased appendix. Patients who have suffered severely from exophthalmic goitre never become as normal as before the disease occurred, but they are a great deal nearer normal than if they had not been operated upon.

I would ask you to bear in mind two points. We must visualize a heart and nervous system flooded with toxic secretion, sometimes continued for years. If that toxic secretion is suddenly reduced by four-fifths, the organs quickly show signs of relief—often indeed dramatically. Yet it is unreasonable to expect that their complete recovery—their capacity to stand up against strain—should be other than gradual; it may never be quite complete. But my second point is that, from the time that a sufficient operation is performed, the downward progress of the disease is arrested, the patient feels a different woman, and is on the up-grade all the time. She is conscious of this herself, and it is obvious to her friends.

REFERENCES.

- [1] SCOTT WILLIAMSON and PEARSE, *Journ. Path. and Bact.*, 1925, xxviii, p. 361. [2] BARKER, *International Clinics*, 1924, i, p. 1. [3] DUNHILL, *Proc. Roy. Soc. Med.*, 1912, v (Surg. Sect.), pp. 61-69. [4] KOCHER, *Journ. Amer. Med. Assoc.*, 1907, xlix, pp. 1240-44. [5] DUNHILL, *Intercolon. Med. Journ. Australia*, Melbourne, 1908, xiii.

X-RAY TREATMENT OF EXOPHTHALMIC GOITRE.

Dr. R. W. A. SALMOND.

In the treatment of this condition by electro-therapeutic measures, the following will refer to X-rays. Much would also apply to radium, but of electrical or combined electrical methods the writer is not qualified to speak.

The type of case which in his experience has shown the best result is that of moderate degrees of acuteness and one presenting the classic symptoms. In the majority of these cases there has been definite marked improvement, in a small number a very striking result or no change at all. So far as is known, it is not possible to say beforehand how any case will respond. As regards the improvement, the most obvious effect has been on the general condition, the patient feeling less "nervy" and in a much better state of well-being, palpitation and tremors disappear and the pulse-rate shows a steady drop. The pulse-rate, if taken under suitable conditions, is a rough guide as to progress, though one may find the general improvement marked while the pulse-rate still remains high. The exophthalmos and the thyroid enlargement are often little affected, or affected only at a later period, when the subjective symptoms have cleared up. In one case the circumference of the neck diminished from $16\frac{1}{2}$ to $13\frac{1}{2}$ in. in five months.

After Results.—Patients are kept under observation for several months after treatment is stopped and the results are found to be lasting in the majority, but some do recur and may be treated again.

Preliminary to Treatment.—Foci of infection or intoxication should be looked for in the nose, throat, teeth and alimentary tract and, if found, treated.

Treatment.—Each case should be treated on its merits and no routine treatment laid down for all. The aim should be to get the thyroid gland as soon as is safely possible under the influence of the radiation, X-ray treatment may be begun by applying a Sabouraud dose to alternate lobes (if both are affected) at weekly intervals for three weeks, and after this, doses at rather longer intervals or of less intensity, depending upon the condition of the patient. Though one wants the gland to be under the influence of the radiation, one should not be tempted to begin with too great or too frequent dosage, otherwise the patient's already highly-strung nervous system may be over-balanced. This applies especially to the more acute cases, where treatment should commence with less dosage and be carefully watched. The isthmus, if enlarged, and any persistent thymus, should also receive treatment.

In view of the treatment possibly extending over several weeks, adequate filtration must be attended to and a filter equal to at least 3 mm. of aluminium always used, otherwise telangiectases may occur even several months later. Too prolonged

treatment may lead to atrophy of the gland, with the onset of myxœdematous and other symptoms. The treatment of pregnant cases is not contra-indicated though results are more difficult to obtain. As most of the patients are ambulant, one should impress upon them the need of rest and of taking things in general more easily. The benefit of treatment may be largely, or even completely, counteracted by the accompanying conditions of life, such as domestic worries or a mother having to bring up a fretful infant with insufficient help. These troubles may interfere so much with the treatment that it is little use going on unless they can be removed.

Mild cases, which might be included under the term hyperthyroidism, respond well but they hardly come under this discussion.

Very acute cases, on the whole, do not do so well under radiation treatment. Special care should be taken in these cases owing to their very unstable nervous and cardiac condition. The patient in one such case became maniacal after three treat-

CHART I.

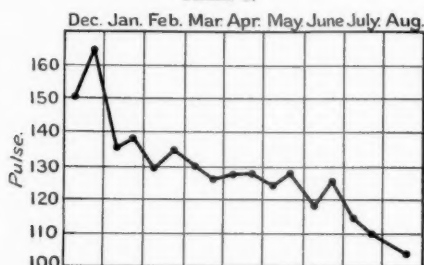
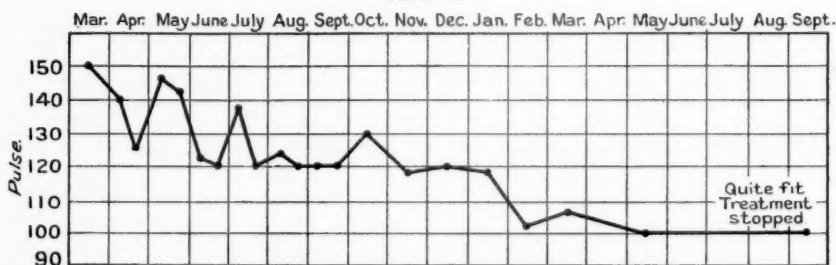


CHART II.



Typical pulse-rate in case under X-ray treatment.

ments at weekly intervals and died, still quite maniacal, within three weeks of treatment being begun. This case may be exceptional but it serves as a warning.

Another very acute case was that of a girl, aged 18, the daughter of a doctor who has kindly given me permission to refer to the case. She was bedridden, pulse-rate 140-160, showed great wasting, had violent and persistent vomiting and was really very ill. After consultation it was decided to place an X-ray apparatus in her bedroom so that even her bed had not to be moved. Within a few weeks the pulse-rate showed signs of dropping; treatment was prolonged, extending over nine months and including thirty-two applications. A very good result was ultimately obtained and the patient is now a normal responsible individual in good health and enjoying life (Chart I).

I have put before you fairly some of the effects, dangers and results of radiation treatment and I hope to have shown that what appear to be cures can be obtained by

this method, though at times it may be slow. If time is an economic factor, then operation should be considered, especially in view of the more recent preliminary iodine treatment.

One cannot help feeling that the definite improvement coinciding with treatment in the cases shown is no mere chance due to spontaneous recovery.

Radiation treatment may be combined with medicinal treatment, but all these cases whose charts have been shown were treated entirely by X-rays. This method of treatment therefore still holds a place in the treatment of Graves' disease in suitable cases; it gives good results in the majority, effects apparent cures in many, and is practically devoid of any risk.

Sir LENTHAL CHEATLE K.C.B. (Chairman)

said that the opening speakers had given very learned disquisitions on the subject from different points of view. It was rather terrible to be one of those persons who were always chiefly influenced by the last speaker. To hear Dr. Salmond speak of the value of X-rays in exophthalmic goitre made one almost a convert to the method. As a matter of fact, he (the speaker) did not like operating on a case which had been subjected to the rays; the operation seemed to be thereby made more difficult on account of the gland then being more adherent to the surrounding structures. He was not a great believer in the value of X-rays in the treatment of exophthalmic goitre. There was a great difference of opinion and diversity of view over the whole world as to the treatment of this disease. In the Eastern and Central parts of America, which he (Sir Lenthal Cheatle) had visited last year, the main function of the physician and his allies seemed to be to prepare cases for the surgeon. The operation very much in vogue there was to excise the whole gland except a posterior film of it; that left sufficient for the patients to live upon, and it got rid of the great risk of accidentally injuring or dividing the recurrent laryngeal nerves. On the other hand, there were people who—with a still small voice—maintained that operation for the condition was completely unnecessary. Some, such as Dr. Barker, were great authorities, and they said that by careful dieting and attention to focal sepsis and rest, a cure resulted.

Even in these discussions finality would not be reached, but it was only by such discussions that medical men would come to appreciate how much—and how little—they knew.

Professor G. R. MURRAY, M.D.

said the ground had already been so fully covered that, at this stage of the proceedings, he would merely make a few remarks on the subject as it had been dealt with.

He was particularly interested to learn the results of Professor Fraser's experience from the intensive study of the group of cases described by him. Further investigations of this kind were practically only possible in a medical unit such as that which Professor Fraser so ably directed. It illustrated the great value of the medical units such as were now in operation in London. He wished to remind Fellows, however, of the valuable clinical studies of a small group of cases which were made some years ago by Dr. Arthur Maude when he was in practice at Westerham; some might remember the series of papers Dr. Maude issued as a result of the study of the cases day by day. Those contributions served as a model of the good work which could be done by a man in country practice if he were so minded.

His own experience had been gathered in the ordinary way from hospital cases, not studied so closely as were Professor Fraser's, and from a number of brief observations on cases seen in practice. He differed from Barker's view as to the duration of the disease, that under any treatment cases would recover in two or three years. He (the speaker) found there was an enormous difference in the duration of the disease in different people.

He remembered two extremes. One was the case of a hospital nurse, who had a typical attack, and recovered completely in nine months so that she was able to take a post as sister in a children's hospital. The other case was that of a lady with severe exophthalmic goitre, which lasted nine years, though she was under ideal conditions, and was able to carry out everything which was advised. Here again, after that long time, there was complete recovery. He saw her nine years afterwards, and then she had developed carcinoma of the breast, and the growth was removed. She said that after recovering from the exophthalmic goitre she had the best health she had ever enjoyed.

With regard to the subject of classification, which was dealt with by Professor Fraser, he agreed there was much to be said in favour of using the term "thyroid intoxication," or "thyro-toxicosis"; he (the speaker) used the term "hyperthyroidism" because he took the view that the symptoms in these cases were due to a great excess of the normal secretion of the gland, not to the presence of a new ingredient in the secretion which did not occur in health. That matter was at present being investigated in America, and until it was proved that there was an added ingredient, the term "dysthyroidism" was premature. The term "thyroid intoxication" had the advantage of including both points of view, and so was beyond controversy. In making a clinical classification it was convenient to take first well-marked Graves' disease. It had long been recognized that this might occur either in the usual primary form, or in the secondary form in a patient already goitrous. In his experience, this secondary form of Graves' disease was much less common than was the primary. During eleven years, in 300 private cases, he had seen only twelve secondary cases. The other forms of thyroid intoxication might be either primary as in simple hyperthyroidism, or secondary as in toxic adenoma, in which latter the goitre had been present a considerable time in a quiescent stage, before symptoms of intoxication appeared. But these groups were not sharply demarcated; there were intermediate cases, simple thyroid intoxication apparently merging into the full disease. With increased knowledge he thought it would be possible to classify these types more exactly, particularly when their life-history could be followed out to the end.

Professor Fraser was correct in his statement that the cause of the disease was not yet known, but he (the speaker) wished to lay particular stress on a very important exciting factor, i.e., emotional stress. In his series of 300 cases, there was a history of sudden shock in thirty-eight, and of prolonged anxiety in seventeen, so that emotional stress was present definitely in 18 per cent. of the cases. He thought it must be an important factor in originating the disease.

Infections—especially influenza—were also important as aggravators of the disease, though he had not satisfied himself that they played a very important part in the original causation.

He agreed that the most important element was early diagnosis. That point did not arise in the class of case generally seen in hospital; they had usually got long beyond the early diagnosis stage. But in this connexion he wished particularly to urge on those in general practice that they should be constantly on the alert for early signs of simple hyperthyroidism, so that prompt measures could be adopted. Often the hopeful stage for carrying out medical treatment had been passed. Cases should not be diagnosed as mere neurasthenia until a proper examination had been made.

The value of rest had been rightly insisted upon, but a very important matter in this connexion was to lay down strict rules on this point, regulating the whole mode of life, not being content with the general exhortation to rest as much as possible. It must always be remembered that this was a disease of long duration, and that as hospitals could not keep the patients very long, most of the time must be spent in the home. This made the treatment of some cases very difficult, because, for economic reasons, the requisite rest could not be secured.

He also agreed that diet should be liberal, as these patients were known to lose a great deal of body-weight, which was regained during the process of recovery; one of his patients had gained 4 st. in weight under X-ray treatment. He had warned his patients not to take much red meat or meat extracts, and this advice was founded on the experiments of Dr. Chalmers Watson. He showed that in animals a diet of this kind induced changes in the thyroid gland very similar to those observed in it in Graves' disease. The main point concerning the diet was that it should be ample, and of it, milk was a valuable ingredient; this should be taken in considerable quantities in addition to the ordinary food.

Under any form of treatment, a gain in body-weight and a fall in the pulse-rate were valuable signs of improvement.

With regard to strictly medical treatment, much had been said concerning iodine, especially in preparing patients for operation; but, in his experience, the effects of iodine were transient; it was like pouring oil on troubled waters; it produced a calm, during which operation could be carried out more safely. But where the treatment was to be medical, the improvement produced by iodine was only temporary. He did not care very much for iodine as a routine measure of treatment. It was yet to be learned which of the cases could take iodine with advantage; he had seen patients made worse by iodine injudiciously given. Iodine, however, had been useful in dealing with the crises which often occurred in this disease, and during which there were times of real danger to life. During these crises he had found great benefit result from the rectal injection of half a pint of warm water, containing a drachm each of sodium bicarbonate and glucose every four hours, and from the application of cold over the goitre.

When vomiting was pronounced, it could be controlled in some cases by morphine or pituitrin given hypodermically, or by 5 gr. of chloral hydrate given in a cachet at intervals of six hours. Still, a certain number of patients died during these acute exacerbations.

His experience of radiological treatment had been similar to that of Dr. Salmond; that in certain cases there were striking results from it. Of medical means he considered X-rays were the most valuable we possessed. This method acted very much better in early stages and in the cases described as simple hyperthyroidism. A number of cases submitted to this treatment made a complete recovery without relapse, and remained well for years afterwards. In a series of 100 cases, many of which had been under his own observation, and were reviewed by Dr. Barclay and Dr. Morrison, they found that 76 of them, after X-ray treatment, either recovered entirely or improved sufficiently to lead an ordinary life. When the review was made all those 100 patients were living. But he would say, also, that the rays were apt to fail in certain cases, particularly in those cases of Graves' disease in which the goitre was larger than the average. The patients, in the majority of cases of typical Graves' disease, had not a very large goitre, but there were cases in which it was unusually large, and in such there was not a good response to X-rays. The same applied to radium, but radium was dangerous in acute cases; it might dangerously over-stimulate an active thyroid, so that the patient suffered from an acute crisis. One patient died after an application of radium, and he attributed the death to that treatment. With X-rays there was less risk of that happening. X-rays seemed to be a sound method of treatment, because their application inhibited over-activity of the active secreting cells, and led to fibrosis and shrinkage of the gland. In a case in which a normal thyroid had been accidentally irradiated in treating a carcinoma, the normal gland was destroyed, and the patient developed myxœdema afterwards. That seldom happened, however, in the treatment of Graves' disease.

The only case in which he remembered having seen that happen was that of a medical man who had Graves' disease, and who urged the radiologist to give him stronger doses than

would have been given in the ordinary way, as he was anxious to get well. His persuasions were yielded to, and he developed myxœdema in consequence, but he took thyroid extract and was now well and back at his practice, though he had to continue taking thyroid, and probably would have to do so for the rest of his life.

He generally advised the use of X-rays for at least two months to begin with, and, if improvement had set in during that period, to persevere with the treatment so as to secure its full benefit. To do this it must be kept up for two years, at intervals; in the later period it was enough to give one application in two or three months, so as to prevent relapses taking place.

With regard to drugs, their value was for symptomatic treatment: quinine hydrobromide, glycono-phosphates, arsenic and bromides all had their use. Digitalis had little effect on the heart until signs of cardiac failure and auricular fibrillation or œdema appeared. It was then valuable when given in full doses.

Mr. Dunhill had dealt with the indications for operation in the condition. His own experience of the operation was from seeing cases under his colleagues who did the operations. The patients in the first three cases for whom he advised operation died within an hour of its performance, and that result, of course, checked his enthusiasm for operation for some time. He found that in his hospital cases he had recommended operation in one in twelve cases. From the physician's standpoint, in selecting cases for operation all the circumstances had to be taken into consideration, particularly the economic position of the patient. There were patients who were bound to earn their living, and whom one would advise to run the risk of operation when, if the same patient had happened to be in comfortable circumstances, one would have recommended her to wait. In all cases, however, in which there was compression of the trachea, operation should be done. In primary Graves' disease operation was indicated when the goitre was unusually large. Cases which failed to respond to X-rays usually failed also to respond to other forms of treatment, and so should be operated upon early. When no improvement followed six months of medical treatment, he agreed that the question of operation on such patient should be fully considered, and it should be carried out if the surgeon and physician agreed about it. His difficulty had been in getting surgeons to operate in cases which he thought needed it, but perhaps Mr. Dunhill's remarks would put heart into many surgeons. The anæsthetist, also, was apt to support the surgeon in his attitude that the operation was too dangerous. Surgeons, he suggested, should think less about their percentages. He believed they were becoming more courageous about doing this operation now that they recognized that valuable lives could be saved by it.

In secondary Graves' disease and in toxic adenoma radiological treatment was apt to fail, and therefore operation should be done early.

Dr. DOUGLAS WEBSTER.

RADIATION TREATMENT IN EXOPHTHALMIC GOITRE.

It is very difficult to assess the value of any form of treatment in diseases such as exophthalmic goitre in which there is much variation in severity, and tendency to natural cure or relapse, and in which some cases pursue an even or mildly fluctuating course for years, while others are so acute that their course may be measured in days or even in hours.

The different views as to suitable treatment must depend largely on the average type of case seen. Generally speaking, surgeons and radiologists see worse cases than physicians and general practitioners. To take extremes, how different must be the opinion as to the general severity of the disease held by Sir William Hale-White, who found, on an analysis of a large series of cases, that 50 per cent. were cured by rest and medical measures (with only a slight tendency to relapse), as compared with the opinion of Crotti as to its severity, for Crotti has performed thyroidectomy, and often thymectomy in addition, "in every case that has come his way."

The radiological view as to treatment, now based on thousands of treated cases, may be said to be, that of those patients who are *not* cured by medical measures only a small percentage cannot be relieved by radiation, while a large percentage are cured.

My own experience of X-ray treatment has been of 168 cases, from which, unfortunately, thirty-seven must be excluded owing to insufficient "follow-up." (It would be very useful if our hospitals would establish "follow-up" departments similar to those established recently in a few American hospitals.) Twenty-four cases are also excluded as they are now under treatment, all improving. Of the 107 remaining, eighty-eight showed marked improvement, a percentage (82 per cent.) similar to some of the results reported by other radiologists. Eleven were males. Four were acute cases, and all these did very well, reacting promptly; one was back to work in a month. Of those in whom treatment had only been begun, or who did not respond promptly, six were operated upon, and of these six two died of the operation. Slight improvement was noted in seven cases; in only six of those who had had six or more treatments, and were followed up, was there no sign of improvement; several of these had marked nervous symptoms, and were placed in unsatisfactory living conditions.

The X-ray techniques advised are very various. On the one hand there is the small repeated dose method; for example, Fischer's, of giving ten small doses within three weeks, then a three weeks' pause; then ten small doses as before and three weeks' pause; then ten again and a three months' pause; then ten again if necessary—thirty to fifty radiations in all.

On the other hand, Nordentoft and Blume have given single large doses, repeated only once to three times if necessary. In many of their 100 reported cases, a single treatment was sufficient for cure. The first of these extremes—many small doses—is very troublesome to the patient; the second appears to me to be risky, as an undesirable or even dangerous reaction might be produced. A single massive radium dose has been followed by acute exacerbation with a fatal result, and with a non-malignant condition no risk is justifiable that can be avoided. I have not employed any of these extreme dosage systems, but have used various techniques; first a small weekly dose method, increasing the interval gradually; then a larger suberythematous dose repeated three- or four-weekly; and lately I have used a method of attempting to "half-saturate" the thyroid with cumulative doses in the first month or two; then, as progress is established, the intervals have been gradually increased to months. In this way a number of patients have recently been restored to health with only about $2\frac{1}{2}$ H. doses—to each side of the thyroid, if large, or to the whole gland from one or other side, if small,—repeated in five to eight treatments in all, taking two to four months for great relief or for cure. For very small thyroids I use 1 mm. Al. filter, for moderately enlarged ones 3 to 4 mm. filter, and for large hard glands 0.5 mm. zinc filtration: in each instance giving a dose about a half to two-thirds of the dose which will produce an erythema on the sensitive skin of the exophthalmic patient: their erythema dose is about 60 to 70 per cent. that of the average skin small erythema dose.

I have not used radium, as the Middlesex Hospital radium is so much "booked up" for cases of malignant disease. But Abbe, Aikens, Dawson Turner, Burrows and others have reported good results. The radium techniques recommended differ very much: quantities from 10 mgm. to 500 mgm. element being used, either close to the surface, or at 5 to 6 cm. distance, or buried in the gland.

As to radiation treatment causing adhesions and hindering possible later operation, I have an open mind on the subject: there is rather a conflict in the literature as to facts and opinions; von Eiselsberg was one of the first to raise the objection, but Holz knecht has said rightly that adhesions, if due to radiation, should be anterior rather than posterior, as the back of the thyroid, with the usual near medium voltage technique, has a considerably less dose than the front. To avoid the possibility in

cases in which operation is in the balance a two or three months' trial of radiation may be made without much risk of causing adhesions with the usual mild technique. If distance doses and high-voltage treatments are given for medium or small thyroids the risk would be greater. In large gland cases a choice should be made, if possible, between operation or radiation, and one or other method adhered to for whatever result there may be.

It is well known that X-ray private cases on the whole do better than out-patient hospital cases, because the home conditions are more suitable, and, as a rule, they can obtain rest and quietness while the treatment is in progress and the disease is active.

The only anxiety in undertaking any new cases lasts during the first weeks, when a suitable dose and dose-method is being chosen for the particular patient. I have seen stimulation effects, due to insufficient dosage, in patients referred to me who had begun to undergo treatment elsewhere. Towards the end of the treatment it is sometimes very difficult to know when to stop; when in doubt a few months' rest should be given. I have seen slight myxoedematous changes appear towards the end of a course of treatment; in every such case, however, the pendulum has swung back, when treatment was stopped, to an approximately normal thyroid balance. I think the best results are obtained when there is a gain in weight to slightly above the patient's previously normal weight.

The first symptoms of improvement are generally seen in the nervous system; sometimes after one treatment benefit is noticed; sometimes the pulse-rate comes down very quickly, in others it takes some months to reduce, though the patient feels well; the exophthalmos and thyroid enlargement remain to some degree in most of the long-standing cases. In more acute cases not supervening on an old goitre the eye symptoms and thyroid enlargement may become normal.

As to local results, I have had no case of burning. Slight telangiectases have been seen in three or four cases where the method of employing doses just suberythematous has been kept on too long, or where insufficient pauses have been made as improvement has begun to be evident.

Interesting points for discussion arise as to the response to radiation of predominantly vagal or sympathetic types of case, and as to the rôle of the thymus. Many radiate the thymus, as a routine, together with the thyroid. I have only given thymus radiation when there is not the expected response with thyroid treatment; or when marked myasthenia, coarse tremor, lymphocytosis with leucopenia, and amenorrhœa, added to a predominantly vagotonic type, all suggest that there is a considerable thymic element in the case. Of the patients who die at operation so many succumb to "thymic death" that thymic radiation might well be given where possible as a routine before thyroidectomy; X-ray examination may be helpful in the diagnosis of thymus enlargement or substernal thyroid.

Surgery had a thirty years' start of radiology in the treatment of exophthalmic goitre; but thyroid surgery has been fortunate in remaining almost entirely in the province of experts, whereas anyone, medical or lay, who has access to an apparatus can give X-ray treatment! Further, X-ray dose measurements only passed the elementary stage in the last fifteen or twenty years. Hence many X-ray failures! It is regrettable, however, that books, even such as Crile's, should be still disfigured with pictures of X-ray burns on the neck; such photographs are as meaningless now as old operation statistics would be. And, from the radiological point of view, it is deplorable that Crotti in his book should devote 606 pages to a consideration of the thyroid, and dismiss radiation with a table of old statistics, and a third of a page of print, ending up with the entirely erroneous verdict that "even in the most competent hands, complications, such as burns, may occur." A statement like this should really not have appeared in a book dated 1922.

In conclusion, it may be said that radiation is one of the few therapeutic measures which have stood the test of time. It stands well in the forefront among the 239 different drugs and other remedies for the disease which were collected by Marine.

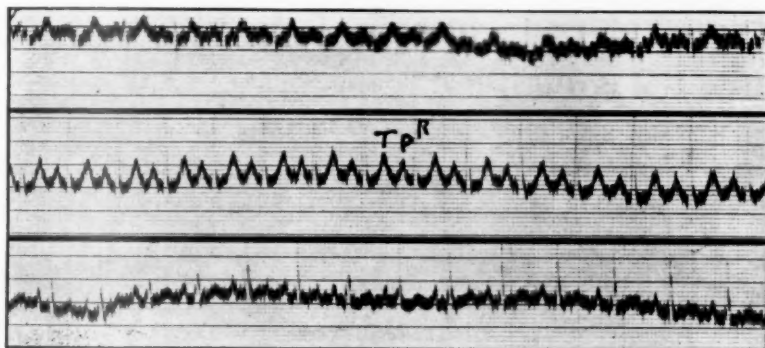
[March 10, 1926.]

Chairman—Dr. HUGH THURSFIELD (President of the Section of Medicine).

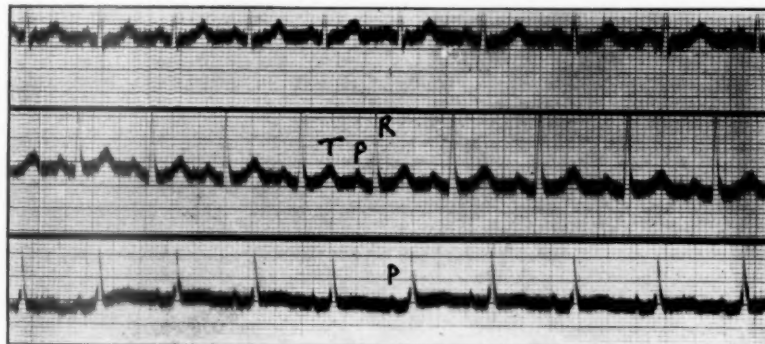
Dr. JENNER HOSKIN.

My remarks are based on 130 cases of primary and secondary Graves' disease which I have examined, both clinically and electro-cardiographically, during the past eighteen months. All but ten patients were women. The ages ranged from 13 to 60. Of these, fifteen were treated medically, nine of them having a serious condition of the myocardium. Of these 130 cases, in 49 per cent. the myocardium was healthy, in

CHART I.



B. P. (1) March 12, 1925.



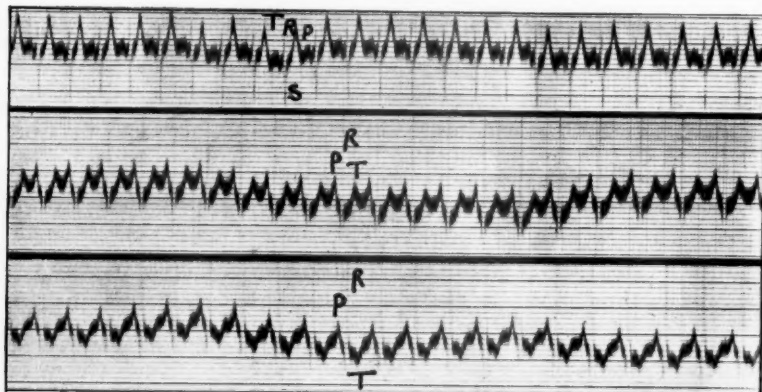
B. P. (2) December 3, 1925.

51 per cent. it showed definite damage. Of those with a healthy myocardium 56 per cent. were under thirty years, of those with a damaged myocardium only 28 per cent. were under 30.

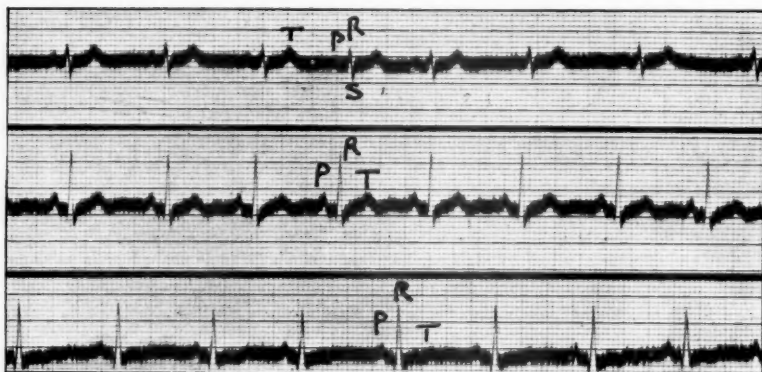
This, I think, is an indication that operative procedure is conducted under more favourable circumstances during the earlier decades, and that it is inadvisable to persist too long with medical treatment in cases which do not respond rapidly.

In one old-standing case in which there had been X-ray treatment some years previously, with marked diminution in the size of the gland, there was a rapid irregular heart with auricular fibrillation and extensive damage to the heart-muscle. I found that the heart condition depended on the severity of the disease and on its duration. A severe onset, such as might occur from shock, especially seemed to affect it. On the whole, however, a moderately severe condition of long duration appeared

CHART II.



L. A., December 10, 1924.



L. A., June 4, 1925.

to have a greater and more lasting effect than did a severe one of short duration. The presence of tachycardia causes a tumultuous heart action, which in time is followed by fatigue and dilatation, with tonic murmurs at apex and base and often a friction rub over the latter. Hearts in the worst state were found in cases of secondary Graves' disease of long duration.

I found great variations in the blood-pressure. Dr. Strickland Goodall states that in primary Graves' disease it is low. In my cases there were only ten cases of 120 or below, the majority being between 130 and 160. In only two cases did the blood-pressure reach 200. The secondary Graves' disease showed a relatively higher pressure than the primary, though in a few cases of severe primary Graves' disease it was found to be very high. The electrocardiogram differs in the primary and secondary cases, though there are cases in which the records approximate as do the two varieties clinically.

The electro-cardiogram changes are:—(1) increased rate; (2) the auricular or "P" wave is usually larger than normal in leads 2 and 3, the P-R interval may be greater than one-fifth of a second; (3) the "T" wave is large or normal in lead 1, normal, smaller than the corresponding "P" wave, or inverted in lead 2, and usually inverted in lead 3; (4) the "QRS" complex is usually normal in shape; (5) in 60 per cent. there was no preponderance of either side of the heart, in 30 per cent. there was left side preponderance, in 10 per cent. right side. Cases with left side preponderance were found usually with raised blood-pressure. Those with right side preponderance were seen in those goitres causing embarrassment to the venous return from pressure on the great veins—the "pneumo-mechanical heart" of Goodall.

In cases of primary Graves' disease the electro-cardiogram curves are normal in direction and amplitude, the "T" wave being upright and larger than the "P" wave in leads 1 and 2, and there is no damage to the conductive system through the auricle. In secondary Graves' disease cases the curves are often altered: the "T" wave is subnormal, diphasic, or inverted in lead 2, and smaller than the corresponding "P" wave. The "P-R" interval may be lengthened. The heart-rate is usually less than in cases of primary Graves' disease.

The clinical findings of the heart support those of the electro-cardiograph in the great majority of cases.

The procedure adopted at the Royal Free Hospital is the following: Cases of primary and secondary Graves' disease admitted with a view to operative treatment are given a few days' rest in bed under administration of Lugol's solution, 5 minims, t.d.s., and in almost all cases the basal metabolic rate is estimated on admission and again before operation. I may add that I am in complete agreement with Dr. McNee, that the pulse-rate is a very fair criterion of the amount of thyroid activity in these cases.

My advice to my surgical colleagues as regards operative treatment is summed up in the following points:—

- (1) No contra-indication to surgical procedure. It is the practice of both Mr. Joll and Mr. Norbury to remove three-quarters to seven-eighths of the gland where there is no contra-indication.
- (2) Not too extensive an operation.
- (3) Primary ligation of one or more thyroid vessels.
- (4) Preliminary rest in bed from one to three months either with iodine medication or with cod-liver oil and malt.
- (5) No operation advisable.

The following points have guided me in advising treatment:—

- (a) Cardiac failure requires preliminary rest in bed and digitalis.
- (b) A systolic blood-pressure over 160 requires either a preliminary rest in bed, a primary ligation, or a modified enucleation, depending on the height.
- (c) Auricular fibrillation, which occurs mainly in cases of secondary Graves' disease of long duration, is not *per se* a contra-indication to operation, but I think it advisable to recommend ligation first.
- (d) For a basal metabolic rate over plus fifty, which tends to persist in spite of rest and iodine medication, primary ligation is indicated.

(e) Marked changes in the form of the electro-cardiogram point to a toxic state of the heart-muscle, and in these cases I advise either a few weeks in bed and administration of cod-liver oil, or a primary ligation, according to the severity of the case.

(f) An electro-cardiogram showing no abnormality beyond tachycardia does not *per se* increase the operative risk.

I have had the opportunity of re-examining a good many cases some months after operation, and have found that the improvement in the general health corresponds with a return to a more normal electro-cardiographic record.

I have found that the cases which have done best are those of toxic goitre, provided that the heart has not been allowed to become too damaged before operative treatment is carried out. In cases with auricular fibrillation the heart has frequently recovered its normal rhythm.

It is remarkable to note what an enormous improvement takes place in many cases even after a primary ligation, and I am inclined to think that except in those cases in which the myocardium is healthy and the hyperthyroidism of only moderate degree, primary ligation is the proper procedure.

I am showing the following electro-cardiograms to illustrate the changes found in cases of primary and secondary Graves' disease and the improvement which takes place after operation.

Case I.—Female, aged 15. Primary Graves' disease. Partial thyroidectomy. First electro-cardiogram just before operation. Second electro-cardiogram three months later.

Case II.—Female, aged 30. Primary Graves' disease. Superior thyroid arteries ligated. First electro-cardiogram just before operation. Second electro-cardiogram, nine months later (Chart I).

Case III.—Female, aged 33. Primary Graves' disease. Double ligation. First electro-cardiogram just before operation. Second electro-cardiogram six months later (Chart II).

Case IV.—Male, aged 19. Secondary Graves' disease. First electro-cardiogram, September, 1924, ligation December, 1924, partial thyroidectomy February, 1925. Second electro-cardiogram two and a half months later.

Case V.—Female, aged 47. Secondary Graves' disease. Disseminated sclerosis began three years previously. First electro-cardiogram with four weeks' history of Graves' disease, Second electro-cardiogram two months later shows auricular fibrillation.

Case VI.—Female, aged 46. Secondary Graves' disease. Superior thyroid arteries ligated. First electro-cardiogram just before operation. Second electro-cardiogram four and a half months later.

Case VII.—Male, aged 13. Goitre for two months with tachycardia but no exophthalmos, showing prolonged P-R interval.

Mr. LIONEL NORBURY

said he wished to lay stress on a procedure in this disease which seemed to be of great importance, namely, primary ligation in some severe cases of the disease in which there were marked cardiac changes. He had carried out this primary ligation in a fair number of these severe cases, and his opinion was that it made the subsequent operation much safer. There were certain arguments for and against primary ligation. One of the main arguments used against it was that it rendered the subsequent operation more difficult owing to the adhesions which had been set up. That was true, but against that there must be set off the fact of the greater safety, and in comparison with that fact the adhesions did not count for much. He could remember two good examples in which, if primary ligation had not been done and a lobe had been removed straight away, a disaster would have occurred.

One of them was the case of a man aged 56, who developed Graves' disease acutely. He was in Burma with his wife, when his native servants attempted to kill them by drugging. He recovered from the effects of the drug and found his wife lying apparently dead by his side. That gave him a great shock, and he noticed that his eyes were protruding at that moment. A month later he had developed goitre. When he (Mr. Norbury) saw the man three months after the shock, the patient's condition was serious: there were present a rapid pulse-rate, very marked cardiac changes, and a basal metabolic rate of 65 to 70. He carried

out a primary ligation, ligaturing one superior thyroid one week, and the other vessel a fortnight later. The patient went into the country and took things easily for three months and he then said he felt much better and able to do most things which he could not do before. His basal metabolic rate had now gone down to -9. This seemed curious, and the physician who did the electro-cardiographic examination asked him (the speaker) not to do anything more in the way of operation for the present. It was now nine months since the ligations were done; the patient was very much better, and living very much the life of an ordinary person, though he was not quite cured. If one lobe had been removed in the first instance, he doubted whether the man would have survived to have another lobe removed.

He had also had a case of similar nature in a girl, in whom there were marked cardiac changes and thyroid intoxication. Both her vessels were ligated. Two months later she seemed to be very much better when she presented herself for inspection. He (Mr. Norbury) wondered whether he ought to do any more for her, but she said she would prefer to wait. She added that she had been to a spiritual healing service and had felt much better ever since! When asked whether he thought the service was the cause of the improvement, he replied that surgery ought to be given at least some of the credit.

Except for the mention made by Dr. Hoskin, nothing had been said in this discussion about primary ligation for goitre, but it was, he thought, a very important matter to consider. Some authorities said that it was useless and should not be done, in fact that it had done harm, as it made subsequent removal of the lobe more difficult. Such a statement he regarded as unnecessarily dogmatic; his own view was that primary ligation had a place in the surgery of the condition.

Dr. W. LANGDON BROWN

remarked that in the course of this discussion Dr. Ryle said he attached more importance in this disease to optimism than to iodine; his (the speaker's) suggestion to him was that he might try both.

In this debate there had been a tendency to minimize the psychological element in these cases. Someone had said that the cause of exophthalmic goitre was "sex and sepsis," and he (Dr. Langdon Brown) could not help feeling there was a good deal of truth in that. It was when a psychical strain was superadded to a septic factor that this syndrome was likely to develop. In hospital work it was very difficult to glean much of the psychological factor.

He gave instances both from hospital and private practice in which the source of psychic trouble had been discovered.

Such cases had impressed him with the importance of the psychological factor, and he felt that if medical treatment was early and efficient, surgery was less often necessary. Though he said that, he had been deeply grateful for Mr. Dunhill's help in difficult cases in which operation was needed.

With regard to the septic factor, he had been much impressed with the importance of tonsillar sepsis. In the discussion on focal sepsis he was surprised to hear Professor Murray say he had not been struck with the influence of tonsillar sepsis in these cases; but that removal of tonsils was not sufficient to effect a cure he (the speaker) agreed. Still, he thought that, in the majority of cases, removal of the septic process played a very important part in the treatment of the disease. Beyond that, as far as medical means were concerned, he had come to rely mainly on rest and the treatment of the psychological factor—though often that was not possible; also on the use of quinine hydrobromide, as recommended by McCarrison, and the application of iodine. And, dating from the time of the observations of Calvert and of Lawrence, when he had been unable to stabilize the patient's weight he had frequently had recourse to insulin.

On the opening day of the discussion, Dr. Graham showed a chart of a case of his (Dr. Langdon Brown's) in which a crisis had occurred. In that case iodine had been withdrawn rather too soon, because the pulse-rate was increasing in spite of iodine.

At that stage the dose should have been cut down, not stopped. And he thought that crisis might have been further precipitated by the use of ergotamine. Ergotamine had been recommended because it inhibited the motor and secretory effects of the sympathetic while leaving its inhibitory effects undisturbed. A few days after it had been given in this case the crisis occurred: it might have been either *post* or *propter hoc*. When the crisis did occur, 10 minims of tincture of iodine were given every four hours, and then there followed a distinct and rapid improvement.

Dr. THURSFIELD (Chairman) asked Dr. Langdon Brown to state what were the indications for the use of insulin.

Dr. LANGDON BROWN (in answer to the Chairman) said he had already mentioned one of the indications. He had generally used it in cases in which he had been unable to check the loss of weight, and he was now using insulin for many conditions, such as anorexia nervosa, when the loss of weight could not be otherwise counteracted. Dr. Eason had intended to take part in this discussion, but was unable to; he had been much interested in that gentleman's communication to the Association of Physicians at the Edinburgh meeting, on the help the pulse pressure might give in determining whether the basal metabolic rate was increased, as it was difficult for the ordinary practitioner to determine that directly. A pulse pressure well over 40 was rather suggestive that in these cases the basal metabolic rate was increased, and he had confirmed the relationship by having the metabolic rate determined. But the converse could not be relied on, for he had had cases in which the pulse-rate was not increased, but the basal metabolic rate was definitely increased.

In cases of enlarged thyroid, in which one was doubtful whether to class them as hyperthyroidism or not, Dr. Gardiner Hill showed that the metabolic rate indicated whether one was dealing with hyperthyroidism or hypothyroidism; and in such a case observation on the difference between the systolic and the diastolic pressures would be a very useful preliminary observation towards determining the point.

Dr. J. W. McNEE

said he wished for a moment to draw attention to one point which might be important in view of our ignorance of the causation of exophthalmic goitre. There was in the Museum of University College Hospital the thyroid gland of a fœtus delivered from a woman suffering from exophthalmic goitre. The fœtus showed all the main features of Graves' disease—prominent eyes and enormous thyroid gland. This specimen seemed to show that the disease might be transferred from mother to child *in utero*.

He wished to refer again to the mild crises, with exacerbation of symptoms, which were common in exophthalmic goitre. Warning of an approaching crisis was often given well in advance of the event by a sudden increase in the pulse-rate and sudden rise in temperature, best seen in patients under treatment with small doses of iodine. In such circumstances the iodine dose should be increased. He agreed with Dr. Langdon Brown about the psychological factor in the ætiology of these crises, and referred to the frequency of sudden exacerbations after "visiting days" in the hospital wards.

Earlier in the discussion he had noted in one chart shown by Mr. Dunhill that two operations were performed on one patient at an interval of twelve days only. He (Dr. McNee) wondered if it was often necessary to operate in two stages, especially since the use of iodine as a preparation for operation had become well known. He would also like to know the factors which determined the surgeon to stop the operation after removal of one lobe, and subsequently proceed to another operation in twelve days. He (Dr. McNee) had formed the view that after iodine

preparation one lobe and a large part of the second lobe could, if necessary, be removed at a single operation. It was a real difficulty if the patient must be told that she would have to undergo two operations.

Dr. THURSFIELD (Chairman)

said he hoped that when Professor Fraser replied he would refer to recurrent goitre in young women during periods of lactation. He did not know what was the basal metabolic rate of such women. He also was somewhat still in the dark concerning the insulin treatment. He would like to know what effect insulin had on the blood-sugar curve in patients who were not suffering from glycosuria.

Dr. H. E. B. CALVERT (replying to the Chairman on the suggestion of Professor FRASER)

said he used insulin in these cases because of the antagonistic actions between the insulin and the thyroid. In a number of these cases there was hæmoglycæmia, which he was able to control with insulin. Later he found that in cases which showed hyperglycæmia and glycosuria, if one pushed carbohydrates, even without giving insulin, the hyperglycæmia often disappeared, as also did the glycosuria, and the patient put on weight. But when the excess carbohydrate diet was removed, there was a tendency to relapse. More rapid assistance was rendered subsequently by giving small doses of insulin. Often the giving of insulin meant taking the burden off protein metabolism and putting it on to carbohydrate metabolism; i.e., taking it off the thyroid and placing it on the pancreas; a strain was placed on the pancreas, and that was covered by giving insulin. He found that large doses did not accomplish more than small doses, namely, 5, 10, to 30 units in twenty-four hours. In one or two cases in which a crisis was threatening—one patient was bordering on the maniacal state—the patients made a rapid recovery merely upon being given insulin, though once the severe symptoms had been controlled, the insulin lost its effect, and so iodine was given. And, although the protein was withdrawn from the diet for the time being, the patients did not seem to suffer. He used the blood-sugar estimation in the ordinary way to check the carbohydrate storage and metabolism. One object of treatment in Graves' disease was to cause the patient to put on weight, and he agreed that insulin had that effect. He had found that in most cases of exophthalmic goitre there was a hyposecretion in the stomach, and that both in them and in normal people injection of insulin caused an increased secretion of gastric juice. It increased appetite and promoted the utilization of carbohydrate; in those directions it was beneficial.

Professor F. R. FRASER (in reply)

reminded Fellows that when he opened the discussion he stated he had had no experience of treating the disease by X-rays and by insulin. X-ray treatment had had able exponents, but except for Dr. Calvert's contribution little had been said of the place of insulin in the management of exophthalmic goitre. During the discussion there had been remarkable unanimity as to what was meant by exophthalmic goitre, and how in general the cases should be managed, but when it came to the details of treatment and to the prognosis in the different types of cases the discussion had not been easy to follow. There appeared to be no agreement as to what was meant by primary and what was meant by secondary Graves' disease. Until there was agreement on the differentiation of types it would not be possible to compare notes on treatment. The sooner an acceptable differential classification was advanced the more rapidly would treatment, both medical and surgical, advance.

Dr. Hoskin appeared to imply that heart-block, or some degree of prolongation of the P-R time, was a typical manifestation of thyroid intoxication of the heart. If so, this was the first time that such a statement had been made. If Dr. Hoskin could accumulate and present further evidence of this it would be a work of value.

Dr. McNee had insisted on the need for anticipating and preventing the exacerbations which were frequently due to emotional causes. The dose of iodine should be increased when an exacerbation seemed imminent, and this applied to those exacerbations due to sepsis as well as to those of emotional origin.

The sexual events of life were important in this disease. Frequently the disease showed exacerbations, and sometimes it appeared to commence, at the time of changes in the sex organs—adolescence, menstruation, pregnancy, lactation and the menopause. There was not sufficient evidence to justify the statement that these events were causal, but they were certainly of importance in the production of exacerbations.

Dr. R. W. A. SALMOND (in reply)

said he was very pleased to hear Professor Murray speak of his experience in the X-ray treatment of the disease. He (the speaker) agreed, in general, with the Professor that very large goitres did not do so well under the rays as the smaller ones. But he failed to agree with Professor Murray's statement that radium was more stimulating than X-rays in the very acute cases; the fatal case he himself (Professor Murray) referred to was no doubt due to the effect of X-rays. If, after consultation, it was agreed that a very acute case should be treated by irradiation, he would prefer radium, because it could be applied without moving the patient, and its application was quite noiseless, whereas there was a definite noise associated with X-ray treatment, which might be disturbing to patients so sensitive as they were in these cases.

Professor Murray referred to the danger of myxœdema following excessive or over-enthusiastic treatment by irradiation. That was a real danger, but fortunately it seldom occurred. Another, but less known danger, was that of rheumatoid arthritis, probably due to the loss of thyroid secretion in the general body metabolism.

Professor Murray laid it down, roughly, that X-ray treatment might be tried for two months, and if there was no improvement in that time, some other method, such as operation, might be tried. Much could be said for this, but in some cases though little response was observed in two months, perseverance ultimately brought about a good result.

Dr. Webster raised the question of the varying techniques, and referred to a case which was cured by a massive dose of X-rays given at one sitting. He (the speaker) had never tried to cure a case of exophthalmic goitre in one sitting. In some acute cases one might use small doses of the rays, in the hope of avoiding over-stimulation of the gland. At hospital he had been asked to give, against his better judgment, ten full skin doses of the rays in ten days. The result was good, but still he did not feel he ought to have taken the risk; the skin was, of course, heavily protected.

Dr. Webster also spoke of a persistent thymus in association with exophthalmic goitre. This was not as well recognized as it might be. He had seen cases which were "hanging fire" during treatment by irradiation to the thyroid gland, and after finding out that there was a persistent thymus, irradiation of that gland brought about a decided improvement.

Dr. THURSFIELD (Chairman)

said that a number of questions occurred to him which he might have put had he been present on the previous day. One was as to whether any surgeon had tried the effect of X-rays applied after the first operation on the gland.

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Section of Anæsthetics.

President—Dr. F. E. SHIPWAY.

DISCUSSION ON ANÆSTHETICS IN CHILDREN.

Dr. HAROLD SINGTON.

THE subject of my opening address is a special branch of general anæsthesia.

In general medicine it has been pointed out [1] that to consider the child a miniature adult is to court disaster; that, in fact, the child, by process of development, alters so entirely that he presents a different type for consideration as the various stages of growth are passed through. Thus the new-born baby is very different to the teething infant, who in turn becomes the toddler, who again advances by means of further development gradually to puberty; the physiological aspect of the infant being as different from that of the adolescent as are the anatomical structures at these two periods of life. This statement is also applicable to the development of the central nervous system. So much the more nervous and impressionable is the child than the adult that his whole central nervous system is at a much lower stage of stability, and may the more readily be permanently injured by unpleasant experiences during early life than later on. And the psychologists have pointed out how an improper mental stimulus, a fright, or some painful experience, may make such a mental impression on a child as subconsciously to affect him throughout the whole of his life.

It is these considerations that the children's anæsthetist should always have in mind, that no nervous shock or strain to the central nervous system should be ever lightly allowed. And it is to this end that I am addressing you to-night, intending to emphasize those points which can make the giving of an anæsthetic to a child as little troublesome as possible, and minimize the shocks and frights which might otherwise damage his central nervous system. We should use every means at our disposal to be as light and gentle as possible, to encourage the child, and to use only those procedures which will prevent the little patient taking fright or in fact suffering any unpleasantness that can be avoided. No time, patience or trouble should be spared to make the induction of anæsthesia as little disagreeable as possible, and to persuade the child to enter into that state of ease and calm which will prevent the occurrence of unpleasant memories when the anæsthetist's ministrations come back to his mind after consciousness has returned.

And so it should be with the preparation of the patient. The preliminary administration of atropine, when ether is subsequently to be given, is an essential. With adults this is ordered in the form of a hypodermic injection; fortunately this hypodermic injection is unnecessary when the patient is a child, as atropine sulphate, taken by mouth, is equally efficacious in the proper dosage during the earlier years. Surely for the child it must be a bad beginning to the big adventure of an operation that a more or less strange nurse should make an assault by puncturing him with a hypodermic needle. And what an introduction to the nurse, who has only recently been known to the little patient! Just when we want the nurse and the child to become good friends; just when we want the child to have full faith and confidence in the stranger who has come to look after him—that confidence which is so necessary for the successful nursing during the post-operative and convalescent stages—this desirable state of affairs is seriously jeopardized, and

frequently is rendered impossible, by the fright caused to the child through the administration of a hypodermic injection.

For some time now at Great Ormond Street we have given the atropine sulphate by mouth one hour before the anæsthetic is administered and the following dosage is employed:—

Up to 6 months of age	1/300 grain
From 6 months to 1 year	1/200 "
" 1 year " 2 years	1/150 "
" 2 years " 3 "	1/100 "
" 3 " " 6 "	1/75 "

Each dose is made up to one drachm of solution, with water. From 6 to 12 years $\frac{1}{50}$ gr. is necessary; given in two doses of $\frac{1}{100}$ gr. in each, the first, two hours before the operation and the second, one hour before. The children never mind taking it, because it is tasteless: and it is in every way as efficacious as a hypodermic injection, completely preventing that salivation which the ether would otherwise cause.

Fortunately the old fetish of purging before operation has been entirely abolished, I think in all quarters; and the even more unpleasant custom of giving an enema is no longer in vogue; both procedures having passed into oblivion. Also, the old method of starvation has given way to the more rational practice of administering glucose for some hours preceding the operation. So now the anæsthetist goes to the child, who is neither weak nor in an emotional state from starvation and purging, nor already in a state of fright caused by the recent puncture of a hypodermic needle. Thus his task has become in some ways an easier one than formerly.

It would be absurd for me to attempt to make any suggestion to you as to the means which the anæsthetist should employ to obtain the confidence of his little patient. No doubt we are as different from each other as the various children whom we anæsthetize. Obviously each case must be considered on its own merits. But it must be borne in mind that the patient always has a certain apprehension which we have to humour and pacify and this can only be successfully achieved if the child approves of us. Children make excellent patients when once we have gained their confidence. The chief maxims which I would advocate are the following: never be in a hurry and never deceive; always explain and always be patient.

Now our aim is to induce anæsthesia pleasantly; to persuade the child to "take" the anæsthetic voluntarily; and, when once he has begun inhalation, to induce unconsciousness as rapidly as possible, of course so far as is compatible with absolute safety. The best means at our disposal to effect this desirable result is the *ethyl chloride-ether* sequence, and I most strongly urge this practice as being the least unpleasant for the child, as effecting the most rapid method of reaching the unconscious state, and as being wholly and entirely safe in the hands of an expert anæsthetist. Why ethyl chloride has not been more extensively used in this country I cannot understand. I can say emphatically that it is entirely safe when properly administered; that is to say, when that one necessity for all inhalation anæsthetics is complied with—a free airway.

At the Hospital for Sick Children, Great Ormond Street, we began to use ethyl chloride in the dental department in 1904, and in the following year it entirely displaced nitrous oxide gas. It is the ideal anæsthetic for the extraction of teeth in children. An anæsthesia lasting up to 2½ or 3 minutes can be safely and rapidly induced; this gives ample time for the complete clearance of all the teeth. I have administered the anæsthetic many times when six to sixteen or more temporary teeth have been extracted; and these have not been removed hurriedly, because the ethyl-chloride anæsthesia gives sufficient length of time to enable the dental surgeon to proceed with care and deliberation—such an important factor in dental extractions. At Great Ormond Street, since 1905, over 25,000 ethyl-chloride

administrations have been carried out in the dental department alone: and I have personally given 10,000 of these myself. There has been no fatality in the whole series of cases; and I have only twice in my 10,000 cases seen cessation of respiration. In both of these cases the cause of the trouble was due to an inefficient airway during the administration; cyanosis occurred and respiration ceased. An intramuscular injection of camphor and artificial respiration brought about a rapid recovery and the little patient in each instance was entirely well an hour later and went home. I was able to satisfy myself at a subsequent visit on the part of each child that they had not suffered from any bad after-effects.

In the dental department I use ethyl chloride by the closed method. The ease of induction and the very rapid occurrence of unconsciousness in the children were inducements to try it as a precursor to ether on the open gauze face-piece, and I find that it successfully fulfils all the demands for the easy induction of anæsthesia in the children. The method employed does not differ much from that used when the induction was carried out under ether itself. A few drops of essence of orange are put on the gauze. This essence of orange is made with absolute alcohol, and in a few breaths will partially anæsthetize the soft palate. The blanket which covers the child is adjusted around the side of the child's head, to prevent the heavier-than-air vapour escaping below the required level, and it is arranged over the lower half of the face in a hollowed-out manner like an inverted basin. The child, according to instructions, is "blowing the stuff away," and he only smells the orange while the alcohol is rendering the nerve-endings of the palate insensitive. Then 3 to 5 c.c. of ethyl chloride are sprayed upon the gauze. The child does not resent this, because of the palate and the nasal mucous membrane being already partially without sensation owing to the orange essence, and after three breaths (sometimes less and sometimes more) the child becomes unconscious. The blanket is then pulled up higher in order to envelop the head, and is more closely adjusted, while the ethyl-chloride anæsthesia is advanced to the third stage. The stages as described by Herrenknecht, who reported 3,000 cases [2], are the following: (1) the prenarcoctic stage; (2) the stage of excitement; (3) the stage of deep sleep; (4) the postnarcoctic stage, the first three stages merging into one another with great rapidity. It is now time to begin to pour the ether on to the gauze, in small quantities at first to prevent the child "catching his breath," and gradually in larger amounts until the gauze is soaked and the ether anæsthetization is established. The initial use of the ethyl chloride has no bad after-effects because it is so rapidly eliminated, and for the same reason it does not cause vomiting. According to Müller [3] the excretion of ethyl chloride generally takes place through the lungs; and in brief narcosis the vapour is eliminated particularly rapidly through the lungs on account of the looseness of the solution in the blood; the kidneys only enter very slightly into consideration when the narcosis is brief. In fact, it is reported by König [4] that the result of examination of the urine of animals for albumin after anæsthetization by ethyl chloride proved negative in all his experiments. In the ethyl chloride-ether sequence it is evident that the increased respiratory efforts caused by the ether are the means of the rapid elimination of the ethyl chloride, with the consequence that the children thus anæsthetized are not liable to sickness any more than when ether is used alone.

Why I so strongly urge the more general use of the ethyl chloride-ether sequence is because I am most emphatically of the opinion that the proper anæsthetic for children is ether. In fact, I do not hesitate to repeat—nor do I fear adverse criticism for being so dictatorial in the matter—that ether is the "anæsthetic of choice" for children in all cases: the only exception consists in that small number of cases of the type which I am about to mention. But the induction of anæsthesia by ether is not a pleasant one for the child, and takes such a comparatively long time that the little patient is sure to resent it, and thus the anæsthetic will cause

that mental impression of disgust, and possibly horror, which we are endeavouring to avoid.

To induce anæsthesia by chloroform, whether alone or in a mixture, is to run a grave risk, in fact I consider that it is to incur a danger to the child's life and I most strongly deprecate the practice, as indeed I do the use of chloroform with children at any time. When the cautery is to be used, of course ether is put out of court entirely, and in these cases I advocate the use of gas and oxygen in preference to chloroform. To emphasize this point further I may say that the amounts of ether and chloroform which passed through the dispensary at Great Ormond Street in 1924, were—2,006 lb. of ether and 140 lb. of chloroform, that is, about fourteen and a half times the quantity of ether was used than chloroform.

As regards gas and oxygen, I pointed out its advantages in certain operations in a previous paper [5], more particularly in the Rammstedt operation for congenital hypertrophic stenosis of the pylorus, and for acute intussusception. These observations, so far as they apply to cases of intussusception, have been further confirmed by Mr. G. M. Gray in his series of 20 cases [6]. My colleague, Mr. J. Birt, has had such considerable experience of the use of gas and oxygen in these acute abdominal conditions that I am leaving him to give further details of this form of anæsthesia, so I will not enter more deeply into the subject myself. The only figures I will quote are the following: last year, at Great Ormond Street, there were 1,925 in-patient operations, of which 85 were gas and oxygen and the remainder open ether. These 85 cases of gas and oxygen were made up as follows:—

Pyloric stenosis	38
Acute intussusception	3
Acute appendicitis	9
Bone-grafts for congenital dislocation of hip	3
Intestinal obstruction	3
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As the operation for removal of tonsils and adenoids is that most frequently performed on children it is only suitable that I should conclude my remarks by referring to some points which may help in promoting the general comfort of the child and which are particularly applicable to these cases. First, the necessity for *deep* anæsthesia by ether is pronounced: it enables the surgeon to obtain a complete view of the field of operation, renders the tissues lax, is conducive to the minimum of hæmorrhage, and enables the operator to stop any bleeding-point with certainty and at his leisure: it is, of course, absolutely safe, and as it prevents the child from swallowing any blood it obviates post-operative vomiting from that cause. But it must be borne in mind that as the cough reflex is abolished it is absolutely necessary that the throat should be kept completely dry, so that there is no blood about, which can be inhaled into the respiratory tract. For this purpose complete co-operation between the anæsthetist and the surgeon is essential, as by means of swabbing, to keep the throat dry inhalation of blood cannot take place. Also, the dryness of the mouth caused by coagulated blood on the tongue, lips and palate, which is a source of annoyance after the operation, may be obviated by sponging the mouth clean with normal saline at the completion of the operation. Lastly, the children recover from the anæsthetic more quietly, and sleep longer and more peacefully, after the narcosis has worn off, when a sedative is given *per rectum*. For a child of ten years of age, potassium bromide 20 gr. and aspirin 10 gr., in half a pint of normal saline which contains 5 per cent. of glucose, should be given slowly *per rectum* before consciousness returns, as soon as the child is put back to bed.

REFERENCES.

- [1] FREW, R. S., *The Practitioner*, 1925, cxv, p. 56. [2] HERRENKNECHT, "3,000 Aethylchlorid-narkosen," *Munch. med. Woch.*, 1907, liv, p. 2421. [3] MÜLLER, B., "Narkologie." [4] KÖNIG, R., "Die Chloroethylnarkose," *Arch. Klin. Chir.*, 1912, xcix, pp. 147-218. [5] SINGTON, HAROLD, "Anæsthesia for Children," *Brit. Med. Journ.*, 1923, ii, p. 801. [6] GRAY, G. M., "Intussusception," *Lancet*, January, 1925, i, p. 71.

Mr. J. BIRT

stated some of his personal experiences in administering gas and oxygen to children. He said he thought he had given it in more than 300 cases for various operations, but that for which it had seemed especially suitable and life-saving was the modern operation for the relief of congenital pyloric stenosis, in which, since its introduction, the mortality-percentage had very greatly diminished.

A child, during and after the operation, had very little shock so long as any degree of cyanosis had been avoided; by this means anxiety with regard to dilatation of the right heart was abolished. During the induction the natural instinctive avoidance of anything abnormal induced the infant, after the face-piece had been applied, to hold its breath for all it was worth, and wriggle, and roll in its endeavour to avoid the gas unfamiliar to its instinctive selectiveness, the result being that it might become deeply cyanosed and die if the breath-holding was not overcome. Rubbing the child's abdomen during the induction sometimes checked this breath-holding, but usually it was necessary to run into the bag an extra supply of oxygen which would soon induce the child to breathe again. This, however, should be accompanied by the addition of a little ether vapour, derived, not by bubbling from the bottom of the ether bottle, but allowing the gas and oxygen to flow over the surface of the ether. Directly regular breathing was re-established a return should be made to the gas and oxygen alone, using the expiratory valve of the gas-bag as much as possible, so as to have freshly mixed gas and oxygen, which was a better anæsthetic and healthier than that which was re-breathed. Re-breathed gas and oxygen lost their value as an anæsthetic. These procedures required some practice to produce good results; for results which were not definitely good with this anæsthetic must be classified as very bad, since the margin between good and bad was so narrow. On the one hand cyanosis had to be avoided, and on the other an excess of oxygen would soon bring the patient right round. It was very essential that the mixtures used should be introduced close to the patient's mouth and not into the bottom of the rubber bag, as any change necessary must be delivered actually to the patient at that very moment. In abdominal surgery, before the peritoneum was opened, regular breathing must be in progress and ether must be added to render the abdomen soft and to prevent the protrusion of the viscera. Then, again, when the peritoneum was being stitched up also ether must be added to the gas and oxygen.

It was important to remember that the anæsthesia which was too shallow would not only hamper the surgeon, but would also allow the shock of the operation to enter the nervous system and so prejudice the chances of recovery.

Gas and oxygen was an excellent anæsthetic for many operations on children, but its use entailed great vigilance on the part of the anæsthetist—not to speak of the very many duties his hands and eyes were required to perform respectively, in order to keep the complex apparatus running well and to watch the condition of the patient at the same time. Another point which was of great importance was to make sure, before starting, that all the cylinders were full and in good working order, and if one were going into the country to have double sets of glass bottles, which formed an essential part of the apparatus. A rubber face-piece was not always as soft as it might be and he (the speaker) therefore advised the use of a thick piece of Gamgee tissue with a small hole in it, and preferably wetted, applied between the face-piece and face to act as a buffer. He had also given gas and oxygen with excellent results for orthopædic operations, including congenital dislocation of the hip; also for splenectomies, removal of kidneys, appendicectomies, removal of mesenteric glands, operations for tuberculous peritonitis, and for other diseases. But it must be stated that, especially after orthopædic work, it is necessary to put the child under the influence of a narcotic immediately at the conclusion of the operation, otherwise the child will suffer acutely, as he will so soon recover from his anæsthetic.

He emphasized the fact that no cyanosis should be present and the young patient should be kept a nice pink colour the whole time. He also added that the quantity of ether used even in a long operation of an hour's duration probably would not exceed four teaspoonfuls.

Mr. T. TWISTINGTON HIGGINS,

speaking from the surgical point of view, congratulated the Section upon its decision to devote an evening to this discussion, because he felt that, in children's surgery, the administration of the anæsthetic and all it involved, called for a degree of skill and experience comparable to that required for the actual performance of the operation. The child differed fundamentally from the adult in his make-up and in his reactions, and these fundamental differences must be appreciated and catered for in all that pertained to the anæsthetic if the best results were to be ensured. The growing tissues of the child were less resistant to infections and more susceptible to trauma, and for these reasons children's surgery demanded a degree of delicate dexterity and detailed technique, which made it quite a distinctive branch of the parent art. In the same way the delicately balanced metabolism of the child was more readily upset by mental and dietetic disturbances and the tissues were more vulnerable to toxic bodies, among which anæsthetics must be counted. Taking all these points into consideration, therefore, the anæsthetist shared with the surgeon a special responsibility in the surgical procedures of childhood. The two must understand each other and their common problem. He heartily endorsed all that had been said by the opener of the discussion in regard to the preparation and general management of the child. The method he had outlined showed that the modern anæsthetist recognized that his responsibility ceased—not when his patient left the operating table, but only when the effects of his anæsthetic on the patient's tissues had finally passed away.

Considering the individual anæsthetics in use, he subscribed heartily to the condemnation of chloroform. He had no hesitation in saying that practically every true anæsthetic disaster he had seen had been due either to chloroform or to "light anæsthesia"; usually a combination of the two. He regarded ether as the anæsthetic of choice for general purposes. N_2O and oxygen had helped greatly in the class of case which Dr. Sington had indicated. He was quite satisfied that it had been an important factor in improving the results of the Rammstedt operations for pyloric stenosis in infants. These cases were specially unsuited to ether or chloroform as the infant was a starved subject with a highly vulnerable liver-cell. In two of his early cases anæsthetized with ether, Dr. Donald Paterson had demonstrated the fatty changes in the liver at the subsequent post-mortem examinations. Since that time he had always employed either local anæsthesia or N_2O and oxygen, and of these, the latter was, in his opinion, far the better.

He asked whether there were any lines along which they might hope for the advent of further improvements in the administration of anæsthetics to children. He supposed they might visualize the ideal anæsthetic as one which inflicted no psychical injury, exerted no toxic effect upon the body tissues and which provided the surgeon with the precise anæsthesia which he required.

The psychical aspect, which had been emphasized by the opener of the discussion, was unquestionably of the greatest importance in the child. A rude mental shock inflicted at a tender age might have a more far-reaching effect than was commonly understood. Every buffer that the anæsthetist could devise was eminently desirable. For this reason he had welcomed the preliminary use of ethyl chloride as described by Dr. Sington. He was convinced that the well-nigh instantaneous loss of consciousness induced thereby was of the greatest advantage to the child. He had been impressed by the rapidity and simplicity of recovery in the cases in which the ethyl chloride-ether sequence had been employed.

With regard to the toxicity question, preliminary preparation, the abolition of starvation and purgatives, the giving of glucose and alkalis, &c., had certainly cut down the risks in this direction, but it seemed to him that efforts such as those described by Mackenzie Wallis and Hewer, to produce a really non-toxic anæsthetic were all valuable, especially in the case of children.

In considering the possibility of improved methods of administration in individual cases, he felt that there were certain operations in which surgeon and anæsthetist might still be more mutually comfortable. He had in mind operations on the brain, neck, mouth (cleft palate, &c.), larynx (laryngeal papillomata), and the chest. Intra-tracheal or rectal anæsthesia seemed to him to be indicated in many such cases, but he realized that the technical difficulties must be great in the case of young children.

MR. A. T. PITTS

said that he would discuss the subject from the point of view of a dental surgeon. He endorsed Dr. Sington's remarks as to the usefulness of ethyl chloride for dental operations on children. He had been associated with Great Ormond Street Hospital for nearly twenty years and during the whole of that time only ethyl chloride had been used in the dental department, without a fatality occurring. With this anæsthetic it was possible to get from two to three minutes' good anæsthesia, which gave the dentist adequate time to carry out all extractions required. In his experience, it was impossible to do this with nitrous oxide, which only gave a very brief period of unconsciousness in young children. In institutional practice ethyl chloride was undoubtedly the ideal anæsthetic for dental operations in children. In private practice, with fewer patients, it was possible to use nitrous oxide with success. But even here, unless the extractions were only likely to take a few seconds, he considered that ethyl chloride was preferable.

DR. W. J. MCCARDIE

said that when he administered ethyl chloride he always added ether, and that the addition of a small amount of ether not only promoted safety, but increased the depth and prolonged the period of anæsthesia. He employed the closed method with the use of Ormsby's inhaler together with an enlarged bag.

How did Dr. Sington treat the obstreperous child, especially if the open method of induction were used? He himself in such cases preferred rapid induction, by means of Ormsby's inhaler, with ethyl chloride and ether. Also what preliminary sedatives, if any, were administered?

He did not agree with Dr. Sington's absolute objection to chloroform, and believed that in certain operations of delicacy, e.g., those undertaken for squint, certain brain and mastoid operations, chloroform alone, or in mixture, was advantageous, and indeed, necessary. In most of these operations a light anæsthesia was sufficient and was reasonably safe. Gas-and-oxygen anæsthesia was in most cases a misnomer, as would appear from the accounts read. In abdominal work, at any rate, the anæsthesia indicated seemed to be rather under ether diluted with gas than under gas deepened by ether. He (Dr. McCardie) said he did not see the advantage of placing gauze under the face-piece, and that he believed that the old-fashioned leather face-piece was the best type. He would like to know whether administration of ethyl chloride was taught the dental students and was countenanced by dental authorities in the case of dental surgeons and dentists. For dental work in children under seven or eight years of age he administered ethyl chloride in addition to ether by the closed method, and gas by the nasal method for those older.

Dr. I. W. MAGILL

said that in his opinion more extensive use might be made of endotracheal insufflation anæsthesia in quite young children when the operation involved the head and neck, with the exception of the larynx. He had used the "double tube" method in the case of a number of children under one year of age and found it definitely advantageous.

LADY BERRY

said that over thirty-five years ago ether was used at the Belgrave Hospital for Children as the routine anæsthetic in all cases except those of quite young infants. For tonsils and adenoids a deep initial anæsthesia was demanded and the operation was usually carried out without further administrations. The procedure was much like that now followed at Great Ormond Street, except that Clover's inhaler was used. She came to the Belgrave Hospital as a newly-qualified resident imbued with the then ordinary idea that chloroform was the ideal anæsthetic for children, and was surprised to find how well ether was taken. Though she seldom used chloroform now, she did not think this drug was the deadly poison some of the remarks made would seem to infer. Formerly she had been for twenty years anæsthetist to another children's hospital where chloroform was practically the only anæsthetic employed. There had been no fatality and very few cases causing any anxiety.

Dr. H. W. FEATHERSTONE

pointed out that ethyl chloride should be employed as a "single-dose" anæsthetic. On more than one occasion, as the dental surgeon had not completed the extractions, a further dose of 2 or 3 c.c. was administered, with the result that the child sank again into deep anæsthesia and could not be roused for four or five minutes. He (Dr. Featherstone) said he had had a considerable experience of gas and oxygen, at the Birmingham Children's Hospital, in operations for hypertrophic stenosis of the pylorus, and had found it preferable to employ a very small gas bag, e.g., of half a gallon capacity, in dealing with these tiny patients whose tidal air was of extremely limited volume.

Mr. R. J. CLAUSEN

said he agreed with Dr. Sington as to the usefulness of ethyl chloride. Was its use prohibited at the London Hospital (as he had heard from a colleague), and if so, why? He pointed out that though for dental work in clinics, &c., the closed method was preferable for its speed, vomiting was less frequent after the use of the open method. For dental work in small children he had also frequently administered nitrous oxide by the nasal method, with good results. Dr. Sington had not said much about maintenance of anæsthesia; at the Queen's Hospital for Children, ethyl chloride open ether was used as a routine anæsthetic for induction, after which he (the speaker) preferred to employ ether vapour with oxygen. He said that he also agreed with Mr. Magill as to the value, in many types of case, of intratracheal ether.

Section of Anæsthetics.

President—Dr. F. E. SHIPWAY.

Apnœa, Dyspnœa and Cyanosis in Relation to Anæsthesia.

By M. S. PEMBREY, M.D., and F. E. SHIPWAY, M.D.

PART I.—PHYSIOLOGY, BY M. S. PEMBREY, M.D.

ANÆSTHESIA is a pathological condition, but, as in other pathological conditions, the process has its representation in physiology; it is impossible to discover any change which is unique. It is the same life and the same death which the pathologist and the physiologist observe; the difference is found in the conditions of the subject and the mental attitudes of the observers. For these reasons a mutual benefit results when anæsthetists and physiologists compare their findings. In this paper it is proposed to restrict the comparison to the subject of respiration.

In the first place apnœa will be considered. The modern significance of the term is an absence of the respiratory movements whereby the lungs are ventilated. In the foetus a long and profound apnœa is the normal condition for some months before birth; all the so-called mechanisms for pulmonary ventilation are present, but in reserve. If the foetus be born two or three months before full term, the co-ordinated rhythmic processes of inspiration and expiration can be established efficiently. The fact is beyond dispute, but not the explanation. It is difficult to understand how such a complex series of movements can suddenly arise in response to the need of air to breathe. In muscular work the general rule is progressive training, trial and error, but here in the first breath might appear an exception. This difficulty has been removed by Ahlfeld [1], whose observations have been confirmed by others. He recorded rhythmic muscular contractions of the human foetus within the uterus; these shallow movements appeared to be respiratory in nature and to arise from stimulation of the medulla by gaseous changes in the blood. The objection that amniotic fluid would be drawn into the lungs is of little import, for it would only pass in and out of the naso-pharynx and is sterile and isotonic. It is possible also that reflex inhibition may occur if the fluid penetrates too far. Moreover, it is known that the foetus swallows amniotic fluid.

Cohnstein and Zuntz [2] removed a foetal sheep from the uterus without damage to the circulation through the placenta; they found that stimulation of the skin, even blowing air into the nostrils, did not cause respiratory movements, but evoked only general reflexes. The premature lamb sucked the experimenter's finger when it was placed in its mouth, and from time to time spontaneously moved its body, but did not draw a single breath until the umbilical cord was tied.

Undue importance has been ascribed to cutaneous stimulation as a cause of the first breath. An infant born in the tropics draws its first breath as readily as one born in a temperate climate or in the Arctic regions. Ahlfeld has shown that infants delivered into a bath at the temperature of the mother's body do not delay their first breath. Breathing by the lungs may commence when the head is in the genital canal: in cases of very protracted labour the full-term foetus has given respiratory movements inside the uterus, for after death amniotic fluid, foetal hair and meconium have been found in the trachea and bronchi. On the other hand, it is well known that, if the placental circulation be intact, the foetus may be subjected to much manipulation in cases of complicated labour or false presentation without being stimulated to breathe prematurely within the uterus.

Cutaneous stimulation can be regarded only as exerting an accessory influence upon the respiratory centre. The effective stimuli are found in changes in the composition of the blood, an increase in the tension of carbonic acid, a decrease in

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that of oxygen. The equilibrium between acid and base in the blood is maintained by constant adjustments; the respiratory movements are an expression of one of these processes—the removal of carbonic acid.

The excitability of the respiratory centre is low in the foetus and the infant, for they show a greater resistance to lack of oxygen and accumulation of carbon dioxide than does the adult. A cat will not survive submersion in water for three minutes, but a kitten two days old will recover after it has been under water for as long as twenty minutes. The young mammal retains characteristics of its cold-blooded ancestors. These old experiments [3] have a practical importance in their application to cases of suspended animation in infants at birth.

There is further evidence that apnoea signifies diminished excitability of the nervous system and the absence of sufficient carbonic or other acid to stimulate the respiratory centre; at the same time the evidence shows that apnoea is not due to an excess of oxygen. In hibernating mammals [4], such as the dormouse, hedgehog, bat and marmot, the respiratory movements are different in type according to the activity and temperature of the animal. In the torpid animals with a temperature below 12° C. there are long periods of apnoea lasting several minutes and broken only by a few respirations; in the inactive animal with a temperature rising above 13° the periods of apnoea become shorter and the periodicity that of Biot's type [5] with a sudden commencement and cessation of breathing, or the Cheyne-Stokes type with a gradual waxing and waning. During these stages of hibernation the excitability of the animal is profoundly depressed, but there is no relaxation of muscular tone; on the contrary, a rigidity which in some respects resembles that observed in some men during the unconsciousness produced by lack of oxygen.

During sleep Cheyne-Stokes breathing is observed in healthy infants and should be regarded as a physiological condition. The same type of breathing has often been noted in old people during sleep, and here again its significance may have no relation to disease, but to a diminished excitability of the nervous system.

It is well known that morphia will produce periodic breathing, often Cheyne-Stokes in type, and in this connexion it is interesting to recall the old treatment, making the patient walk about whether he will or not. The success of this treatment can now be explained as due to the production of carbonic acid in sufficient quantity to stimulate the depressed respiratory centre. Yandell Henderson [6] in recent times has shown the value of the administration of oxygen containing 5 per cent. of carbon dioxide to patients poisoned with morphia. In some places it appears to be the routine practice to give patients an injection of morphia some time before the induction of anaesthesia; the drug depresses the excitability of the respiratory centre, and in patients who are especially sensitive to the drug it may give rise to serious failure of respiration.

The injection of adrenalin into anaesthetized animals will sometimes produce Cheyne-Stokes respiration. This condition, according to the investigations of Ff. Roberts [7], is due to want of oxygen produced in the respiratory centre by vasoconstriction.

The classical type of periodic breathing called after the names of Cheyne and Stokes is observed in some forms of heart disease and arterio-sclerosis. The periods of apnoea alternating with periods of waxing and waning respiration can be abolished most readily by air containing 3 or 4 per cent. of carbon dioxide, more slowly by high percentages of oxygen such as 80 or 90, or even by a deficient supply of oxygen, such as 12 per cent. Analyses [8] of the alveolar air of the lungs show in typical cases a low tension of oxygen and a high tension of carbon dioxide at the beginning of the period of breathing, and the opposite during the last waning breaths. Such results indicate that this periodic breathing is due to a diminished excitability of the nervous system associated with a defective supply of arterial blood; the carbonic acid accumulates and the oxygen diminishes until the nerve cells are stimulated,

the waxing respirations begin and culminate in hyperpnœa or dyspnœa, whereby a large quantity of carbonic acid is washed out and sufficient oxygen is taken into the blood; apnœa follows owing to the absence of an adequate tension of carbonic acid to stimulate the respiratory centre. The inhalation of air containing more than 2 per cent. of carbon dioxide abolishes apnœa by maintaining the tension of that gas in the alveolar air and the blood at its stimulating value. The administration of pure oxygen by means of a mask and valves abolishes apnœa by maintaining the partial pressure of carbonic acid in the blood at its stimulating level; the respiratory centre is no longer excited by lack of oxygen to send out the forcible impulses which had previously resulted in excessive ventilation, whereby carbon dioxide was washed out of the alveoli and the blood. Air containing a smaller percentage of oxygen than that present in atmospheric air abolishes apnœa; the constant deficiency of oxygen stimulates the respiratory centre.

The same type of breathing has been observed in healthy men after ascents to high altitudes, especially when their excitability was reduced by sleep. Experimentally, as Haldane and Douglas [9] have shown, it is possible to induce this periodic breathing in healthy men by a lack of oxygen due to re-breathing expired air deprived of carbon dioxide by soda lime.

In hysterical patients Cheyne-Stokes respiration has been observed; it can be abolished by suggestion.

There remains for consideration another type of apnœa which was described by Noël Paton [10] and F. M. Huxley as the postural apnœa of diving birds. When a duck is held with outstretched neck in the posture for diving, all respiratory movements are inhibited and a long period of apnœa is the result. The afferent impulses in this reflex arise in the muscles of the neck and in the labyrinths, for the apnœa cannot be produced if the corresponding nerves be divided.

A reflex inhibition of respiration, it would seem, is the chief factor leading to anoxæmia and death in cases of drowning in a few inches of water. The immersion of the face in a depth of water sufficient to cover the nose and mouth appears to start the sequence of events, whether the act be voluntary as in a case of suicide, or involuntary in epileptics or accidents to healthy subjects.

The apnœa which can be obtained by forced breathing enables a man to remain under water a long time after a dive; this, however, is a dangerous proceeding and has been attended by fatal results in some cases, the diminished excitability produced by the removal of too much carbonic acid causing anoxæmia, unconsciousness and death.

Forced breathing washes out carbon dioxide and produces the condition of acapnia, to which Yandell Henderson [11] has especially directed the attention of anæsthetists.

As long ago as 1876, Addinell Hewson [12] of Philadelphia, published in the *Transactions of the International Medical Congress* a paper on the analgesic effects of rapid breathing; he gave an account of his experiments and the operations which he had performed upon his patients during this condition. He found that breathing at a rate of forty or fifty per minute for three to five minutes was necessary for the production of the desired degree of analgesia. The condition was recognized as one of cyanosis by the colour of the patients' lips and cheeks and the blood which escaped during operations. Muscular rigidity was in some cases very definite, in others very slight and transient. The induction of this state he considered to be due to a "diminution in the respiratory function, a cutting off of the normal supply of oxygen and retaining the carbonic acid in the blood to be sent to the nerve centres."

The occurrence, causation and significance of apnœa in health and disease have been considered in detail, because the condition is one of fundamental importance in relation to anæsthesia. The respiratory movements are not only an indication of the ventilation of the lungs, but also of the excitability of the nervous system and

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the circulation and composition of the blood; they afford more varied information to the anæsthetist than an examination of the pulse.

The counterpart of apnœa is found in the difficult and laboured respiratory movements which constitute dyspnœa. The former, as we have seen, indicates the absence of stimulation; the latter is evidence of vigorous excitation of the nervous system. Similar factors are concerned, for the effects of oxygen and carbonic acid are relative to their tensions and the excitability of the nervous system.

During running an athlete passes through a stage of hyperpnœa followed by dyspnœa, but if in spite of distress he continues to run at the same speed, an adjustment of the output of carbon dioxide and the intake of oxygen occurs and he obtains what he calls his "second wind." [13] In many contests the condition of the runners at the end is one of anoxæmia.

Cyanosis is a state of anoxæmia, and in its most typical form is seen in mammals immediately after birth. In such cases it is a physiological condition. The disturbance or interruption in the placental circulation has caused a fall in the oxygen and a rise in the carbonic acid of the foetal blood, two factors which will stimulate the respiratory centre and start the ventilation of the lungs. This form of cyanosis is well known to gynecologists under the term "blue asphyxia," in contradistinction to "white asphyxia," a condition of anoxæmia accompanied by a failing circulation of the blood.

Sufficient examples have been given to support the contention that pathological processes are not unique but have their representation in physiology. It is now necessary to consider the evidence from the side of anæsthesia. This is given by Dr. Shipway in Part II.

REFERENCES.

- [1] AHLFELD, "Beiträge zur Lehre vom Uebergange der intrauterinen Athmung zur extrauterinen." Festschrift für Ludwig, Marburg, 1890. [2] COHNSTEIN and ZUNTZ, *Arch. f. d. ges. Physiol.*, Bonn, 1884, xxxiv. [3] EDWARDS, "De l'influence des agents physiques sur la vie," Paris, 1824, pp. 629-632. PAUL BERT, "Leçons sur la physiol. comp. de la respiration," Paris, 1870, p. 534. [4] PEMBREY and PITTS, *Journ. Physiol.*, 1889, xxiv, p. 305. [5] BIOT, *Lyon médical*, 1876, xxiii, p. 517. [6] YANDELL HENDERSON, *Journ. Amer. Med. Assoc.*, 1924, lxxxiii, p. 758. [7] FF. ROBERTS, *Journ. Physiol.*, 1921, lv, p. 346; 1923, lvii, p. 405; 1924, lix, p. 99. J. MELLANBY and A. ST. G. HUGGETT, *ibid.*, 1923, lvii, p. 394. [8] NEWTON PITT, PEMBREY and ALLEN, *Med.-Chir. Trans.*, London, 1907, xc, p. 49. PEMBREY, *Journ. Path. and Bact.*, 1908, xii, p. 258. [9] HALDANE and DOUGLAS, *Journ. Physiol.*, 1909, xxxviii, p. 401. [10] NÜEL PATON, *Proc. Physiol. Soc., Journ. Physiol.*, 1912-1913, xlv. [11] YANDELL HENDERSON, *Amer. Journ. Physiol.*, series of papers in vol. xxi, 1908, to vol. xxvii, 1910. [12] ADDINELL HEWSON, *Trans. Internat. Med. Congress*, Philadelphia, September, 1876. [13] COOK and PEMBREY, *Journ. Physiol.*, 1912-13, xlv, p. 429. MACKEITH, PEMBREY, SPURRELL, WARNER and WESTLAKE, *Proc. Roy. Soc.*, B, 1923, xcv, p. 413.

PART II.—ANÆSTHESIA, BY F. E. SHIPWAY, M.D.

A frequent cause of apnœa during anæsthesia is the instruction given to the patient to "breathe deeply." Deep breathing washes out too much carbon dioxide. Respiration should be natural, that is, quiet and easy, and any attempt of the patient to breathe rapidly and deeply in order to obtain unconsciousness in the shortest possible time should be restrained, for it disturbs the natural ventilation of the lungs and the administration. Sometimes this desire arises from nervousness, a feeling of asphyxia, or the memory of a former induction during which this symptom was present. A rapid induction cannot be obtained without a sense of discomfort, for it is impossible to establish rapidly the required tension of the anæsthetic in the blood without cutting down the supply of oxygen and, in the case of chloroform, running the risk of over-dosage.

Apnœa during induction with chloroform may lead to syncope from direct action on the heart, if at the time that breathing is resumed a high concentration of vapour is present and the inspirations are deep. Apnœa may also occur during chloroform anæsthesia, especially in feeble subjects, elderly people, and those who suffer from arteriosclerosis, if the drug be given by the open method. Cheyne-Stokes breathing may be established. It is caused chiefly by the lowering of the arterial pressure

induced by the depressant action of the drug on the heart. The respiratory centre is also depressed and the rate of flow of the blood-stream is lessened. Further, Buckmaster and Gardner [1] have shown that even during light chloroform anæsthesia the oxygen capacity of the blood is reduced by 40 per cent. This action of chloroform is serious, for it increases the tendency to anoxæmia. From all these causes the tissues are starved of oxygen, but, on the other hand, it must be remembered that anæsthesia in itself reduces the metabolism and therefore the tissues do not call for so much oxygen. Oxygen should not in consequence be used as a routine. If Cheyne-Stokes breathing should arise, it can be abolished by giving oxygen or carbon dioxide; the latter can be obtained by substituting a semi-open for the open method. On physiological and anæsthetic grounds the semi-open method makes its appeal.

Apnoea is not often seen when chloroform is given through a tracheotomy tube, a condition in which the dead space is much diminished. The explanation appears to be that, although chloroform depresses respiration and produces anoxæmia, the intake of air is unimpeded and the supply of oxygen is adequate in relation to the rise in carbonic acid. Apnoea as a complication is most likely to arise during the anæsthesia produced by intratracheal insufflation, if the ventilation is excessive and carbonic acid is washed out of the lungs and blood. In a case recorded by Pembrey [2] an average ventilation of 16 litres of air per minute was sufficient to oxygenate the blood, but 30 litres per minute produced apnoea for a period of two minutes; the pulse was very good and the blood-pressure was 155 mm. at the beginning of this rapid ventilation. After a minute it had fallen to 138 mm. During the period of apnoea the pressure gradually rose again to 150 mm. As the tension of carbon dioxide in the blood increased, the patient commenced slow voluntary breathing. A sample of alveolar air taken when respiration recommenced showed a percentage of carbon dioxide of 6.04, which is about normal. Analyses of samples of alveolar air taken during the operation showed that the blood-pressure followed the carbon dioxide tension. It is not advisable to abolish the respiratory movements during intratracheal insufflation anæsthesia, for their presence favours the exchange of gases in the lungs and maintains the action of the respiratory pump upon the circulation of the blood.

During prolonged anæsthesia with gas and oxygen, in which the expired air is allowed to escape through valves, acapnia may occur. This can be abolished by instituting re-breathing, the amount being regulated to suit each case. An excessive pressure of carbon dioxide leads to sweating, flushing, hurried breathing and a falling pulse-rate, while the blood-pressure rises at first but falls later; a deficient pressure produces pallor, a cold clammy skin, feeble breathing and a quickening pulse-rate. This picture is less often seen to-day than in the past, when Hewitt's apparatus, which makes no provision for re-breathing, was used. Acapnia was not uncommon; it produced all the signs of shock, for which indeed it was mistaken. Acapnia leading to apnoea was seldom seen, for lack of oxygen and the formation of lactic acid in tissues stimulated the respiratory centre. Exactly what part lack of oxygen and excess or deficiency of carbon dioxide play in any given case it is difficult to say: the problem is so complex. Bayliss [3] found that if excess of carbon dioxide was given to cats, anæsthetized by urethane, together with excess of oxygen, the first effect was a rise of blood-pressure, but this was soon followed by a fall. On removal of the excess of carbon dioxide the blood-pressure rapidly returned to normal. If there was a deficiency of oxygen, even when the carbon dioxide was absorbed by caustic soda, the blood-pressure did not fall so rapidly, but the fall lasted a very long time and was not recovered from for a long time after a normal supply of oxygen. There was often a permanent failure of the respiratory centre.

The danger of a reduced partial pressure of carbonic acid in the blood is increased during administration of gas and oxygen if at the same time there is a deficiency of oxygen in the inspired air. It is known that as the partial pressure of carbon dioxide

is diminished the hæmoglobin holds on more tightly to the oxygen. Thus a condition may arise in which, although the blood is completely oxygenated, the patient may be suffering from anoxæmia. If the percentage of oxygen in the inspired air falls during the acapnia to about 12, the respiration, which has been shallow, may become deep, for lactic acid formed in anoxæmia acts on the respiratory centre, and on the dissociation of oxyhæmoglobin, in a similar manner to carbonic acid. When morphine or scopolamine has been given, some depression of the respiratory centre exists (although atropine may have been administered at the same time); re-breathing should be instituted almost from the start and the amount increased during maintenance, in order to promote absorption of the anæsthetic. Indeed, in the absence of re-breathing, the respiratory movements may be too slow and shallow to oxygenate the blood, although the percentage of oxygen in the inspired air may be high.

Apnoea seldom, if ever, arises during the administration of ether by the open method, as this method is in reality a semi-open one. Analyses [4] of the air under a mask which was covered with two layers of domette and rested upon a pad placed on the face, ether being given by the open or vapour method, showed that the percentage of carbon dioxide was adequate to stimulate the respiratory centre, but was never excessive. The percentage ranged from 2 to 4.

Hyperpnoea and dyspnoea are quickly produced by an excess of carbon dioxide, which may arise from re-breathing or some obstruction in the airway; in the latter case there is also a lack of oxygen. Obstruction of the airway may exist before anæsthesia. The combined effects of this lack of oxygen and excess of carbon dioxide are so serious that it has been well said that the difficulties and dangers of anæsthesia lie largely above the larynx. No one can study the details of fatalities arising during the administration of an anæsthetic without being struck by the part played in their production by neglect of this truth. Falling-back of the lower jaw, retraction of the tongue, laryngeal spasm, accumulation of secretions in the respiratory tract are serious complications of anæsthesia which throw an undue strain upon the nervous and cardio-vascular systems. Of all these complications the most difficult to overcome is the presence of excessive secretions. A small quantity of mucus which becomes churned up and aerated in the larynx and trachea constitutes a danger, especially if the patient's heart be feeble or dilated.

An excessive secretion in the smaller bronchial tubes is highly dangerous, and its removal presents an almost insuperable difficulty; this is clearly demonstrated by the following case, the notes of which have been given to the author with permission to publish.

A boy, aged 11, was operated upon for acute appendicitis; he looked very ill. The lungs were healthy. Atropine $\frac{1}{16}$ gr. was injected half an hour before induction, which was carried out by chloroform and ether; open ether was then used. About a quarter of an hour after anæsthesia was complete, slight twitchings of the left arm and shoulder were noticed; they spread within a minute to the whole of the body, becoming so violent that the surgeon had great difficulty in closing the wound. The colour of the patient had never appeared really dusky and oxygen did not appreciably relieve the spasms. Chloroform was then given at the request of the surgeon, who thought that the condition was one of ether clonus. About 2 dr. were given, but there was no effect. The pharynx was mopped out, an intratracheal catheter was passed and a little mucus was sucked out and oxygen was given through the catheter. The spasms became less frequent and settled down into definite attacks, which came on every two or three minutes. In the intervals the boy was quiet, his respirations were shallow and at first rapid, but later they became very slow. Rigidity and spasms then started afresh, and this condition lasted for about three-quarters of an hour. The pulse failed rapidly, and in spite of stimulants and massage of the heart the boy died. At the post-mortem examination the trachea and bronchi were found to be clear, but many of the smaller bronchioles were blocked by mucus, the secretion of which had been profuse. Most of the substance of the lungs was purple and congested, but one lobe of the right lung remained pink.

In this case the cause of death appears to have been anoxæmia. Hewitt recorded two similar fatal cases under the term "mucus inundation."

It is not generally realized that excitement and struggling during induction are often asphyxial in origin, irregular strengths of vapour giving rise to reflex phenomena, such as swallowing and breath-holding, or directly to a feeling of suffocation if such concentrations are high. It is known that by the administration of ether by the drop-method, in which is used a very dilute vapour which is very gradually increased in strength, a difficult subject can be made to pass into anæsthesia with very little excitement. Clinical experience teaches also that the free use of oxygen during induction, particularly when cyanosis pre-exists, whether due to obstruction or an affection of the lungs, largely eliminates or cuts short the so-called struggling stage.

The most interesting of the signs of lack of oxygen—interesting because its significance is often overlooked—is the onset of rigidity and clonic muscular movements, which may be erroneously regarded as an indication of light anæsthesia. It has long been known that abdominal rigidity may be due to anoxæmia and may be abolished by restoring the air-way and supplying oxygen. It is not so well known that certain clonic movements may occur during the third stage of anæsthesia, at a time, indeed, when the slackness of the eyelids and the jaws and the absence of the corneal reflex indicate that anæsthesia is deep. The most common of these are piano-playing movements of the fingers and hands, coupled sometimes with jerky adductor movements of the arms: at other times irregular movements of the shoulders and arms are observed. These athetotic phenomena are of great importance; they are due to lack of oxygen and are, therefore, more common during anæsthesia with chloroform and its mixtures than with ether. A recognition of their nature is essential; less, not more, anæsthetic is required and complete ventilation of the lungs must be secured. These movements are more likely to occur in men, and in anæmic and feeble subjects, especially if the induction has been rapid.

Anoxæmia is shown clinically by cyanosis. There are two kinds of cyanosis. In the first, the arterial and venous pressures are raised, and there is great engorgement of the veins. The colour of the face and of the mucous membranes is blue. The right side of the heart becomes over-distended with blood, and cardiac failure may occur. The engorgement is always associated with an excess of carbon dioxide. This condition is relieved by securing free ventilation of the lungs. In the second variety of cyanosis the veins are not over-full and the colour is grey or leaden. This is the more serious condition, for the circulation is failing. It is associated with a deficiency of carbonic acid, and the indications are to give oxygen and carbon dioxide. Insufflation of oxygen through an intratracheal catheter is sometimes used to restore respiration. It must be remembered that this manœuvre may increase the danger by blowing out carbon dioxide at a time when the tension of this gas is already low. Mouth-to-mouth insufflation is sometimes practised. It has Biblical as well as clinical and physiological support (II Kings iv, 32-35). It acts by supplying sufficient oxygen and a high percentage of carbon dioxide, and is a method of restoring respiration in desperate cases of apnœa which deserves to be more widely known. [5] The question whether oxygen shall be given in uncomplicated cases has already been answered in the earlier part of this paper. It is unnecessary; indeed it is possible to give an excessive amount of anæsthetic where the colour of the patient is good owing to the abundance of the oxygen supply. The colour of the blood is an indication of its content of oxygen, but may be no guide to the activity of the tissues. Further, the use of oxygen in uncomplicated cases may tend to disguise a faulty administration.

REFERENCES.

- [1] G. A. BUCKMASTER, *Proc. Roy. Soc. Med.*, 1918, xi (Sect. Anæsth.), p. 15. [2] M. S. PEMBREY, *Proc. Roy. Soc. Med.*, 1914, vii (Sect. Anæsth.), p. 34. [3] Letter to Author. [4] M. S. PEMBREY and F. E. SHIPWAY, *Proc. Roy. Soc. Med.*, 1916, x (Sect. Anæsth.), p. 7. [5] W. H. OGILVIE, *Guy's Hosp. Gaz.*, 1921, xxxv, p. 73.

16 Pembrey and Shipway: *Apnœa, Dyspnœa and Cyanosis*

Discussion.—Mr. S. R. WILSON said that Dr. Pembrey in his nevertheless excellent paper had been rather hard on the obstetricians in belittling their efforts to establish respiration in the new-born child by slapping it. Whilst it was generally recognized that carbon dioxide was the essential respiratory hormone, yet one must still remember it was also possible to influence respiration through nervous channels. It was true that if one did nothing but wait for carbon dioxide to accumulate, respiration would eventually take place, yet the influence of respiration on circulation should not be ignored, and the establishment of a respiration played an important part in filling the heart, especially during anæsthesia. And further, Dr. Pembrey had himself been compelled to admit it, later in his paper, in describing a form of Cheyne-Stokes breathing, which, he stated, could only be neurotic in origin. He was very interested in Dr. Pembrey's remarks on analgesia in relation to forced breathing, for it had been his own practice in the case of young children requiring simple extractions of temporary teeth first to paint the gums with iodine, giving suggestions of painlessness at the same time; then to get the child to close its eyes so as to obviate fear of pain on seeing the forceps, and finally to induce the patient to take deep breaths. He found that under these conditions it was very unusual for the child to experience pain. He was entirely in agreement with the avoidance of morphine before anæsthesia, except in nitrous oxide administrations. He would like Dr. Pembrey's opinion on the periods of apnœa, lasting two to three minutes, which not uncommonly occurred during the extensive modern exploratory laparotomy. As a rule, it caused no anxiety, but if the circulation were becoming affected it was his habit to administer oxygen, containing 5 per cent. carbon dioxide, to establish breathing, or in the absence of this mixture to use a modification of the Biblical method of artificial respiration, by blowing through a yard of rubber tubing into the patient's throat-tube, so utilizing the carbon dioxide in the expired air. He fully agreed with Dr. Shipway's remarks on re-breathing, and on the dangers of obscure accumulations of mucus in the air-passages. Lastly, would Dr. Pembrey make a precise statement as to the cause of fetal apnœa? Was it due to lowered sensitiveness of the respiratory centre, or to a diminution of the CO₂ tension in the blood, or were both factors concerned?

Mr. C. LANGTON HEWER said that he was not quite clear as to whether Dr. Pembrey considered that artificial apnœa produced during endotracheal anæsthesia was detrimental to the patient or not. He had anæsthetized several patients with the endotracheal gas-oxygen-ether method and had kept them in a state of complete apnœa for a very considerable time, in some cases up to an hour, and had never seen any untoward symptoms develop. The colour, pulse-rate and systolic and diastolic blood-pressure remained the same whether the patient was breathing or not. This, he thought, was rather remarkable in view of the stress which physiologists laid on the beneficial action which the changes in intrathoracic pressure, brought about by respiration, exercised on the filling of the heart. If, however, as appeared to be the case, this artificial apnœa was not deleterious to the patient, it was of immense service to the surgeon. In thoracic surgery, the immobility of the lungs might mean that an operative procedure otherwise impossible could be accomplished with ease; and in the more familiar region of upper abdominal surgery anastomoses might be very greatly facilitated if the suture line were perfectly still.

Dr. PEMBREY (in reply) said that he did not doubt that cutaneous stimulation influenced the excitability of the nervous system, but he was nevertheless convinced that the routine practice of slapping the newly born child in order to establish respiration was no more necessary than in the case of other mammalian animals, domesticated or wild. The natural stimulus was found in the increase of carbon dioxide and the decrease of oxygen in the blood owing to the separation from the mother. If a newly born calf did not breathe of its own accord the farmer did not smack or kick its buttocks, but opened its mouth, pulled forward its tongue and blew air from his own lungs into its throat.

Prolonged apnœa during anæsthesia was evidence of a diminished excitability of the nervous system relative to the tension of carbon dioxide in the blood: if the heart were beating strongly there appeared to be no reason for anxiety. In fetal apnœa the essential factor appeared to be the low excitability of the nervous system; this condition of the nervous system persisted for some time after birth and was shown by the fact that the infant spent most of its time asleep and exhibited Cheyne-Stokes respiration.

He was much interested to hear that Mr. Langton Hewer had kept patients in a state of complete apnœa for as long as one hour. During anæsthesia the value of spontaneous respiratory movements was found in their indication of the activity of the nervous system; but, if the needs of the surgeon required such a long immobility of the lungs, the condition of the circulation of the blood would be a guide.

[February 5, 1926.]

Nitrous Oxide: its Impurities and the establishment of Tests Suitable for Official Adoption.

By C. F. HADFIELD, M.D.

IT will probably be within the knowledge of most of those present that about two years ago a Committee, known as the Anæsthetics Committee, was jointly established by the Medical Research Council and this Section of the Royal Society of Medicine to inquire into various points concerned with anæsthetic agents and to stimulate research in such matters. The original suggestion came from the Council of this Section and was welcomed by the Medical Research Council, which was already considering the advisability of some such course. Our Council nominated to serve on the Committee our former President, Dr. Blomfield, our present President, Dr. Shipway, and myself. The Medical Research Council was able to obtain the services of Dr. H. H. Dale, F.R.S., Director of the National Institute for Medical Research at Hampstead, Prof. Donnan, F.R.S., Professor of Chemistry at University College, London, and Prof. Pembrey, F.R.S., Professor of Physiology at Guy's Hospital.

Since its formation the Committee has co-opted Prof. Storm van Leeuwen, of the University of Leyden, as a corresponding member, and quite recently has obtained the assistance of Prof. H. B. Dixon of the University of Manchester. At the first meeting held in March, 1924, Dr. Blomfield was appointed chairman and I undertook the duties of honorary secretary. Up to the present the Committee has held thirteen meetings and as each of these has been of about two hours' duration it will be understood that many matters have been discussed. It might, I think, be not out of place for me to express here, on behalf of Dr. Blomfield, Dr. Shipway and myself, the three representatives of this Section, our appreciation of the very friendly and comrade-like manner in which these distinguished scientific men have worked with us throughout.

The particular reason that first suggested to the Council of this Section the desirability of the formation of this Committee was the fact that for some time various complaints had reached it dealing with untoward clinical results occasionally obtained with nitrous oxide gas. These complaints had been rather vague, but it was felt that there was probably some foundation for them and that in the process of manufacture some impurity might be included capable of producing unpleasant effects. I think it has only lately become generally realized that nitrous oxide is not, and never has been, included in the British Pharmacopœia, and that therefore there are no official tests of purity by which its quality can be judged. This exclusion is difficult to understand, especially as I gather that the object of those responsible for the Pharmacopœia is not to suggest or even approve of any particular therapeutic agents but rather to provide standard methods of preparation and tests for any drugs which, wisely or otherwise, are extensively used by the medical profession. Certainly on this basis nitrous oxide should have gained a place many years ago. The manufacturers of nitrous oxide have very kindly furnished me with confidential figures as to their yearly output, and I am the only person who is in possession of this knowledge. I cannot, of course, give you any idea as to the total, but without betraying trust I may say that I was amazed at the size of the grand yearly total.

There being thus no official standard of quality, I think I am justified in saying that the high quality of the product issued by the manufacturers speaks well for the care they have exercised. At the same time it is to the interest of both manufacturers and users that this anomalous state of affairs should cease. Preparations are now in hand for the issue of the next edition of the British Pharmacopœia, and it should be and, I believe, is the declared intention of the Council of this Section to

press for the inclusion of nitrous oxide in the forthcoming volume. With this in prospect it has been the aim of my Committee to collect all possible information with a view to the formulation of a table of tests suitable for inclusion in the Pharmacopœia. These should be of a sufficiently delicate nature to insure a pure and efficient anæsthetic agent without being so complicated and difficult of application as to hamper their use on a commercial scale.

Unfortunately we are not yet in the position to formulate such a table, although we hope to do so soon. Representatives of the various manufacturers making nitrous oxide have been invited to this meeting and it is hoped they will take part in the discussion. Their views on all points will be valued, and especially those dealing with the commercial applicability of any of the tests suggested. I should like at this point to say that during the past two years I have been in almost constant communication with most of the various firms concerned in the manufacture of nitrous oxide. In each case they have done all they could to assist us and have placed at our disposal much information of a more or less confidential nature. I am sure that I shall not be exceeding my powers if I here publicly extend to them the thanks of the Committee.

I should like to mention one point of personal explanation. Although, as I have said, the work of the Committee is not completed it was thought well to make some sort of report to this Section. This would also offer an opportunity for a general discussion which could not fail to be useful. As someone had to put together an introductory paper I was the unfortunate individual requested to do so. But the duty only fell to me because as secretary I had in my possession all the necessary documents and not because I am in any way qualified to deal with the intricate problems in chemistry and physics which are involved. No doubt many interesting and instructive questions will be asked in the subsequent discussion, but I shall not attempt to answer them. Fortunately, most, if not all, the members of the Committee have promised to be here this evening and they will be able to deal with those subjects which are beyond my powers of explanation. Again, I am attempting to put before you the facts obtained and the views so far adopted by the Committee, and if I am able to interest you in any way the credit will belong to that Committee. My communication, however, is not official and has not been seen by any other member of the Committee. So it may be that I may easily fall into error both as to facts and opinions. If I do so the fault is entirely my own.

As the result of communications to the medical press, the Committee has received a certain number of complaints about unsatisfactory samples of nitrous oxide. Altogether I find that we have received from five separate anæsthetists fairly full details of clinical findings, together with cylinders containing unused remainders of the gas said to be at fault. These, which might be called the "complete cases," have naturally been the more instructive. We have also considered reports—in some cases very full reports—from five other sources, from none of which, however, has the nitrous oxide complained of come into our hands.

Complete Cases.

To deal with the complete cases first. Generally speaking, the symptoms complained of, although by no means identical, exhibit a certain similarity, and it would be wearisome and useless to read to you the details of them all. The complaint, accompanied by the fullest clinical report, was that submitted by Dr. Ramsey Phillips; it was, in fact, the one largely responsible for the institution of the inquiry. I think the best course for me to pursue will be to deal with this report fairly fully and then make brief mention only of the other four.

(1) *Dr. Ramsey Phillips' Cases.*—In October, 1924, Dr. Phillips anæsthetized six patients (four women and two men) with this particular gas for dental extractions. He reports:—

The gas used had a strong smell like brown potash or dirty wash-tub water. Clinically my complaint was that anaesthesia could not be produced without marked cyanosis; this led me to use the conjunctival reflex as a guide, a thing I never do in the ordinary way. This particular cyanosis was unusual. Lividity, white lips, grey colour of the skin, small to medium pupils, eyeballs looking directly forwards, and convulsions quite unlike the usual jactitation. In each case I gave large quantities of oxygen when this occurred, but the recovery was very slow. In some cases I had to re-apply the gas with free supply of oxygen, as I had not allowed the operation to be commenced. Exactly the same thing occurred. There was no observable obstruction to the air-way in any of the cases. On recovery, all the patients felt very poorly, pulse small, irregular and soft. Nos. 1 and 2 gave rise to considerable anxiety at the time. No. 3 felt really ill when there should have been no cause for it. No. 4 also. No. 5 was not a dental case, but was having her neck stretched and manipulated for an alleged dislocation, and the convulsions were put down by the surgeon to his manipulations, who felt rather pleased, I think. No. 6 was badly knocked out, but she was not a good subject for gas. I heard afterwards that she had had a severe cardiac breakdown after it. I have not met with this before or since. My apparatus was in good working order, and in each case there was plenty of oxygen in the oxygen bag at the end of the case. The clinical picture was quite different from the cyanosis and jactitation common in cases where most of the air is washed out of the lungs and no oxygen is given. Again there was the strong smell of the gas, and the conjunctival reflex (taken well away from the cornea) was strongly present up to a point in some cases where I had to desist, and I was unable to say that the patient would not feel the operation. No cough or sign of irritation in the air passages was present, and no nausea followed. I rather naturally dreaded to go to another gas case. I went to the makers and told them about it. While assuring me that the gas was good and normal, they showed me how to smell and taste it, and produced other gas which they acknowledged had no smell, while that which I had been using smelt strongly. I changed my stock of gas, with the exception of the two bottles I sent you. While admitting that these difficulties may have been caused by myself, I felt it would be good to find out if the gas was good for human beings or not, since there are no regulations to control the manufacture.

The unused gas was sent to Dr. King—chemist to the National Institute for Medical Research at Hampstead. I should like to say here that the Committee is very greatly indebted to Dr. King for the prompt and able manner in which he has conducted many analyses dealing with nitrous oxide and also various ethers and other substances.

Dr. King reported as follows :—

It was bubbled through silver nitrate solution. Absence of turbidity indicated *absence of halogens*.

Bubbled through dilute permanganate solution. No diminution of colour observed as compared with control, indicating *absence of reducing substances*.

Passed through dilute litmus solution made up in freshly boiled water. Solution rapidly became red as compared with control. *Acidic substances present*.

Passed through baryta solution. Rapidly became cloudy. *Presence of carbon dioxide confirming litmus test*.

Passed for a long period through ferrous sulphate solution. No darkening observed as compared with control. Hence, *absence of nitric oxide*.

Several qualitative tests showed that, on shaking small volumes, 5 to 10 c.c. with cold water in a eudiometer, there was always a small volume undissolved. Accordingly 500 c.c. of gas were collected over water in a large corked cylinder and shaken with successive portions of fresh water until no more was dissolved. The residual volume was about 12 c.c. This was transferred to a van Slyke gas analysis apparatus and, exposed to alkaline pyrogallol, showed no appreciable change of volume. *Absence of oxygen and carbon dioxide*. The residual gas was not inflammable and did not support combustion. *Absence of carbon monoxide and presence of nitrogen*.

Summary.—The nitrous oxide examined contained a small proportion of carbon dioxide and about 2 per cent. of nitrogen.

A few days later Dr. Dale wrote to me as follows:—

Since the last meeting, King and I have further examined the sample of nitrous oxide received from Ramsey Phillips. We passed the gas through a dilute solution of oxy-hæmoglobin until all the oxygen was blown out and reduction complete. The spectrum was then that of reduced hæmoglobin with only a single diffuse absorption band. This appears to me to exclude CO and NO beyond shadow of doubt, and much more decisively than any animal test could, or any ordinary chemical test. Pembrey agrees, but I am sending him the other cylinder of N_2O , so that he and Shipway may test it on some animals, if they think fit.

King and I also tested the gas further for nitrites, and, as a last shot, for cyanogen—both tests being completely negative.

I think it was the negative result of this very thorough examination that made us realize the difficulty of the question under examination. We had all probably assumed that these irregular manifestations were due to the accidental presence of some obvious impurity such as a halogen, nitric oxide or carbon monoxide. In this case, however, it seemed clear that all such substances were absent. The presence of a small quantity of carbon dioxide can hardly be of any importance, as it would not appreciably increase the percentage normally present in the alveolar air. Even if it did, the trend of modern teaching in anæsthetics seems to suggest that it would be advantageous rather than the reverse.

(2) *Dr. Hugh Powell's Cases.*—Another member of this Section, Dr. Hugh Powell, of Cheltenham, also sent some cylinders of nitrous oxide which had proved unsatisfactory in his hands and in those of Mr. Cade, a dental surgeon. The ill-effects had been noticed in some five or six patients consecutively anæsthetized with the same batch of gas. Here the symptoms were rather different. The patients were not completely anæsthetized—they complained that they felt the extractions but had no pain. The recovery, however, was accompanied by distinct nausea, headache and giddiness. Dr. King reported on the remaining nitrous oxide. None of the expected impurities were found, but there seemed to be a relatively large amount of nitrogen present—namely, 5 per cent.

(3) *Dr. de Caux's Cases.*—Still another member of this Section, Dr. F. de Caux, had a case of a girl who, during a dental extraction, became so cyanosed and breathed in such a shallow manner that artificial respiration had to be used, and she did not fully recover for upwards of an hour. He had noticed that three other patients anæsthetized from the same cylinder had taken longer than usual to recover consciousness. Here again Dr. King's report was much the same. None of the ordinary impurities was present, but there was 3·5 per cent. of nitrogen.

(4) *Dr. Windsor Bell's Cases.*—In July of last year Dr. Windsor Bell had trouble with five cases anæsthetized from one cylinder at the National Dental Hospital. On recovery one woman had a typical epileptiform fit and all the other four showed some convulsive movements during recovery. Dr. King, by chemical tests, was satisfied as to the absence of expected impurities except a small quantity of CO_2 , and this was confirmed as regards CO, &c., by spectroscopic tests with hæmoglobin.

(5) *Messrs. Coxeter's Discarded Sample.*—Messrs. Coxeter kindly supplied us, by special request, with samples of a gas which, although free from all the ordinary impurities, did not in their opinion come up to standard and so was not issued. Dr. King confirmed the absence of these impurities but found that the gas contained about 20 per cent. of nitrogen and 3 per cent. of oxygen. Dr. Shipway used this gas in some experiments on animals and found it satisfactory.

Reported Cases.

(1) One manufacturer, whose name I do not mention, very kindly furnished us with details of all complaints which had been received during the period of years in which he had been making nitrous oxide, and also with the results of the detailed

examination made in each case. It would take too long to go into the particulars of the five or six cases. In most of them nothing was found at all, except sometimes a higher percentage than usual of nitrogen. In one, however, there was a distinct but faint oily smell, the origin of which was difficult to trace. No oil is used in the compression plant and it was suggested that it might have been due to a dirty cylinder.

(2) Professor Karsner, of the Lakeside Hospital, Cleveland, Ohio, U.S.A., has kindly sent us some information about cases of poisoning by nitrous oxide in that hospital; this had resulted in the installation of a very complete plant for making nitrous oxide in the hospital itself. He also mentioned a case where some commercially supplied gas had almost certainly contained nitric oxide.

(3) Dr. Maughan, of Albany Street, London, N.W.1, reported the bad results obtained on anæsthetizing three children (among many) at a School Treatment Clinic. All three cases showed signs of collapse without cyanosis. Being struck by this, in the remaining cases he gave half or three-quarters of his usual dose and obtained good anæsthesia, followed by easy recovery. The remaining gas was returned to the makers and carefully examined by them—one of the partners himself inhaling it. He found it to be chemically quite pure, except that, as is so often the case, it contained some nitrogen.

(4) Almost by accident the Committee discovered that some time before, much trouble had been caused by the action of some gas used at the Physiological Laboratory at Cambridge during some experiments on cats. I have in my possession a large bundle of documents dealing with this case. The findings are, however, so confusing as to be useless, except that they are of interest as showing the confused nature of the evidence one may have to examine. From the report of an inspector, it would appear that the gas used to anæsthetize a cat for a very brief cardiac puncture, rapidly killed the animal. As the cat's hæmoglobin was found to have been changed to methæmoglobin—a change obvious not only in the spectroscope but also to the naked eye—the gas very justly came under suspicion. The remaining gas was analysed by the Public Analyst and found to contain no abnormal constituent. When, further, it was stated that not only other cats but the same cat had previously been anæsthetized satisfactorily from the same cylinder, the problem did not become any more simple. The same batch of gas had been sent by the makers to many other quarters and no complaints were received. The only possible solution that occurred to the Committee was that the outlet of the cylinder had been accidentally contaminated by some strong acid which had been removed before the analysis. The possibility of this was denied by workers in the laboratory. After much correspondence with those concerned, the problem was dropped as hopeless.

(5) A further series of cases was reported to the Committee by the War Office, through the Medical Research Council. These cases, which had occurred at Cologne, were similar to some of the others and not in themselves particularly interesting, as they were accompanied by scanty clinical details. Also, no more of the gas was available for examination and in fact the War Office admitted that the source of the gas was unknown. Before it was reported to us, however, the remaining gas had been most exhaustively examined at the Government Laboratory by Sir R. Robertson and his assistants, and their very full report was placed at our disposal. Here, again, the only fault to be found chemically was a relatively high proportion of nitrogen.

As these cases have passed before the Committee, the members have become impressed by the very frequent finding of a variable percentage of nitrogen in the gas under suspicion. In the Cologne cases this amounted to 10 per cent. Although the exclusion of all traces of nitrogen seems to be difficult, some firms at any rate guarantee their nitrous oxide to be more than 99 per cent. pure. According to a

contributor to an American journal, nitrogen would be formed during manufacture by the interaction of nitrous and nitric oxides in the presence of water, with the additional formation of nitric acid which would be removed by the ordinary scrubbing process. The equation seems to be:—



Now it does not seem likely that the admixture of a small percentage of nitrogen (say up to 5 per cent.) with nitrous oxide will have any very marked effect if that admixture is a reasonably even one. The nitrous oxide will, of course, be correspondingly weaker, but when we consider that nitrogen, by acting as an asphyxiant, would itself have a certain anæsthetic action, we should hardly expect it to be noticeably weaker. That is, of course, if it were given without much air or oxygen. The researches of Sir R. Robertson first directed the attention of the Committee to the fact that, especially with larger percentages, the admixture would not be an even one. Nitrous oxide, as we all know, is easily compressible, and becomes a liquid at a pressure of thirty atmospheres at 0° C. This fact has been largely used by the manufacturers as a test of purity. If their gas liquefies at the usual temperature and pressure, it is probably good gas. If it does not, the process has failed at some point and the gas has to be discarded. Nitrogen, on the other hand, is much less compressible and refuses to liquefy under the processes employed by the manufacturers. If, then, a sample of nitrous oxide containing a percentage of nitrogen is compressed into a cylinder, that cylinder will contain liquid nitrous oxide, while the space not actually occupied by the liquid will contain a high percentage of nitrogen in a gaseous condition. It is possible that a certain amount of the nitrogen would be actually dissolved in the nitrous oxide. As far as I can discover, we have no authoritative statement as to the solubility of nitrogen in liquid nitrous oxide. The point of practical importance is that when a cylinder containing such a mixture is opened, the composition of the gas first issuing from it will vary greatly according to the position in which the cylinder is held. If the cylinder is placed vertically with its mouth downwards (a position we anæsthetists never adopt), the gas should be pure nitrous oxide or nitrous oxide containing only such a proportion of nitrogen as is soluble in the liquid. If the position is reversed and the cylinder held upright with the mouth upwards, it will be the highly compressed but still gaseous nitrogen that will be tapped first, and the resulting gas will be nitrogen with a variable proportion only of nitrous oxide. With the cylinder held nearly horizontally the conditions will be much the same, but will vary according to the actual angle adopted. From this it will be readily understood that a cylinder of nitrous oxide containing an apparently harmless percentage of nitrogen may, under certain conditions, when first opened, yield a gas so rich in nitrogen as sensibly to affect its anæsthetic action. It is, in fact, probable that this relatively high percentage of nitrogen is the explanation of some of the abnormal symptoms that have been reported to us. Some time ago I was discussing the matter with Mr. Trewby, whose skill and experience as a dental anæsthetist is well known. He assured me that we should never find much wrong with the cylinders of gas we examined, as it was always the gas delivered first that caused the unpleasant symptoms. This was an interesting independent confirmation of what we had already learnt from Sir R. Robertson. I should like to add that Mr. Wellesley, of Messrs. Coxeter and Co., also drew our attention to this fact about the same time.

There is another possible cause for abnormal symptoms under nitrous oxide that should be mentioned, although I do so with some diffidence in an assembly such as this. The cause to which I refer is some fault in the apparatus used. I should not dare to speak of this at all were I not ready to admit that I have had bad results from this cause on more than one occasion. The apparatus which we anæsthetists are accustomed to use is dependent on the correct working of delicate valves,

usually made of sheet rubber, and it is very easy for one of these to cease its function without the fault being at once obvious. I have sometimes found that a prolonged induction, or some other unusual symptom, has been caused by the sticking or curling of a valve in my inhaler, and I am sure this must have occurred to others. I do not wish to say that all or any of the cases I have briefly mentioned were due to this cause, but I do think it is a factor which has to be kept in mind. It is a point which has also been politely suggested to me by at least one of the manufacturers.

As the result of the numerous examinations, both chemical and spectroscopic, made by Dr. King and others, I think we are justified in concluding that the gas supplied to us anæsthetists by the three or four firms who make it in this country is a very pure product. We have never found any trace of such poisonous substances as the halogens, nitric oxide, nitric acid or carbon monoxide. There may be a little carbon dioxide which in such small quantities would be harmless, and occasionally a little oxygen of doubtful origin. The only impurity which is at all frequently present is nitrogen. The possible, or perhaps one might say the probable, source of much of this nitrogen, from the interaction of nitrous and nitric oxides in the presence of water, has already been described. We have also seen how even a small percentage of nitrogen may, under the physical conditions obtaining in a nitrous oxide cylinder, as it were magnify itself sufficiently to produce abnormal results when the cylinder is placed in certain positions.

The fact that the gas with which we are supplied is so pure speaks well for the methods adopted by the manufacturers. In several cases we have been informed, in confidence, of all the details of the process used, including sometimes secret "tips" of great utility. There is some variation in the methods, and some firms certainly appear to devote more attention to scrubbing processes than others, and possibly to control the whole plant in a more scientific manner. The end result appears, however, to be much the same. Again, in the testing of the finished product one firm differs from another in its methods and one may be more scientific than another. The fact that a poor sample will not liquefy at the right temperature and pressure seems to be a great safeguard, and in addition some makers inhale samples to see what it smells like—a method perhaps more altruistic than scientific.

While thus, in the absence of any standard or official tests, it must be admitted that we have been well served in the past, it is not less obvious that such tests should be established and applied to each batch of nitrous oxide issued for use as an anæsthetic. I am possibly in error in speaking of batches of gas, as the process may be carried on as a continuous one. In this case standard tests should be applied to the product at certain fixed intervals.

That no such tests exist in England has been already stated. In one of the instances already mentioned the Ministry of Health was involved, and it enumerated some tests taken, I believe bodily, from the Pharmacopœia of the United States. A point that appears to be unnecessarily stressed is that the ammonium nitrate used in the manufacture must be of not less than 99·8 per cent. standard of purity. This would place the responsibility on the 'wrong shoulders and might allow a careless manufacturer to throw the whole blame for his bad gas on the wholesaler who had falsely declared that his ammonium nitrate was of the requisite purity. At any rate from our point of view the purity or impurity of the chemicals used is of minor importance so long as we can be certain that the resulting nitrous oxide is absolutely pure.

The selection of the best and most easily applied tests for nitrous oxide is not an easy task. Such tests should be sufficiently stringent to ensure the absence of all harmful impurities, while at the same time they must be simple enough to be used in ordinary chemical works or in the shop of any pharmacist. I had hoped that we should have made further progress than we have before bringing this matter before you to-day for discussion. A Sub-Committee consisting of Dr. Dale, Prof. Donnan,

and Prof. Pembrey has been working at it for some time and I cannot do better now than close this somewhat discursive account by giving you their preliminary suggestions. Their report is as follows:—

ANÆSTHETICS COMMITTEE.

Sub-Committee on Tests for Purity of Nitrous Oxide.

Professor Donnan, Professor Pembrey, and Dr. Dale met, as arranged, in the National Institute for Medical Research on Thursday, November 26, 1925. Dr. Harold King kindly attended, and gave the Sub-Committee his co-operation.

It was suggested that the tests adopted in the United States Pharmacopœia might be taken as a first basis for the Committee's recommendations. The description given in the U.S.P., 9th Decennial Revision, 1916, is as follows:—

Pass 2,000 mils of the gas, measured under normal atmospheric pressure at about 25° C., through 100 mils of barium hydroxide T.S. at a rate not exceeding 4,000 mils per hour; not more than a slight turbidity is produced (*carbon dioxide*).

No opalescence is produced in a mixture of 100 mils of distilled water and 1 mil of silver nitrate T.S. by 2,000 mils of the gas under the conditions described above (*halogens*).

No change in colour is produced in 100 mils of distilled water, to which 5 drops of litmus T.S. have been added, by the passage of 1,000 mils of the gas through the liquid under the conditions described above (*acids or bases*).

No alteration in colour is produced in a solution of 0.2 mil of tenth-normal potassium permanganate V.S. in 100 mils of distilled water by the passage of 1,000 mils of the gas through the liquid under the conditions described above (*reducing substances*).

Of these tests the only one which fell under criticism, as possibly unnecessarily severe, was that for carbon dioxide, Professor Pembrey maintaining that the presence of a small percentage of carbon dioxide would be advantageous rather than deleterious. The tests do not provide adequately for the detection of nitric oxide, not specifically for nitrogen peroxide, and not at all for the detection of carbon monoxide.

For *nitrogen peroxide* Professor Donnan suggested that the following test should be adequate:—

The baryta solution used for detecting excess of CO₂ should subsequently be acidulated with sulphuric acid. A drop of dilute potassium permanganate solution added to this liquid should not be decolorized. (The test would need to be given in quantitative form, and carried out against a control in which an equal quantity of baryta solution, through which no gas had been passed, would be acidulated, and similarly tested with an equal addition of potassium permanganate).

For *carbon monoxide* two tests came under consideration:—

(1) The hæmoglobin test, which has been used for the Committee.

It was agreed that further experiment would be needed before this test could be described in quantitative form and recommended for adoption. The available data show that not less than 0.07 per cent. of CO can be detected in *air* by the hæmoglobin test. In this case, however, the CO is competing for hæmoglobin against 20 per cent. of oxygen. It seems likely that much smaller proportions of CO in a gas indifferent to hæmoglobin, such as N₂O, could be detected by the production of spectral bands, permanent after the addition of a trace of sodium hydrosulphite, and therefore not due to oxygen. Such a test could be very easily carried out by anybody possessing a small direct-vision spectroscope. It would be necessary, however, to determine the limiting concentration of CO, which can thus be detected.

Professor Pembrey undertook to make some mixtures of N₂O with small measured proportions of CO, and to determine the smallest concentration of CO which could thus be detected.

(2) *The Test using Iodine Pentoxide.*—This test is said to detect as little as 0.005 per cent. of CO, or, in other words, 1 c.c. of CO in 20 litres of gas. The gas is passed through a U-tube containing iodine pentoxide heated in a water bath to 60°-70° C., and the issuing gas is passed through a solution containing potassium iodide and starch. If a blue colour is produced the amount of iodine liberated can be determined with $\frac{1}{1000}$ N. sodium thio-sulphate. It can be calculated that 1 c.c. of CO should liberate rather more than 2 mgm. of iodine, which would require about 25 c.c. of the thio-sulphate solution. Two litres of gas, if containing 0.1 c.c. of CO, should therefore liberate an easily titratable quantity of iodine. This proportion of CO would be physiologically negligible, and the test, therefore, seems to be a perfectly efficient one. A blank control, in which the same volume of pure air was passed through the iodine pentoxide tube, would presumably serve as a preliminary. The test would be rather a cumbrous one for carrying out in an ordinary pharmacy.

Nitric Oxide.—It was thought probable that NO would react similarly to CO with the iodine pentoxide, in which case it would also be detected by the test above described. Members promised to obtain further information on this point, and Professor Donnan offered to have an experiment made. An alternative test suggested for NO was to mix the volume of gas to be tested with a suitable volume of air or oxygen, and, after allowing time for formation of NO₂, to pass the mixture through a solution containing potassium iodide and starch, when any NO should be detected by the liberation of iodine. The test would, of course, also detect pre-formed NO₂.

Test for proportion of N₂O present.—The Committee's work has shown that the impurity most frequently responsible for trouble is nitrogen, which on compression will tend to occur, in higher than the general concentration, in the gas in the top of a cylinder. It is suggested that a sample of gas, taken with the cylinder upright, should contain at least 95 per cent. N₂O.

For the analysis of N₂O, Boothby and Sandiford's method (*Amer. Journ. Physiol.*, 1915, xxxvii, p. 377) is recommended, in which the 10-c.c. gas analysis apparatus is used. 2.5 c.c. of nitrous oxide is mixed with about 7.1 c.c. of hydrogen and burnt, and the contraction of volume noted. If the gas is freed from CO₂ and O₂ previously, the contraction gives the volume of N₂O in the original sample.

Discussion.—Mr. G. WELLESLEY said that in his opinion the method of estimating the percentage of nitrous oxide in a sample by absorbing it with water and measuring the volume of the residual gas was inaccurate. He said that if the impurity was nitrogen, or chiefly nitrogen, this method made the gas appear to be worse than it really was. He suggested that the method of analysis used by Baskerville and Stevenson was preferable.

The tests laid down by the Pharmacopœia of the United States (tenth decennial revision of January 1, 1926) appeared reasonable, except that the one for carbon dioxide was perhaps rather severe, in view of the opinion expressed by several anæsthetists that this gas in small quantities was not deleterious. Among the further tests suggested he thought that an outside limit of 5 per cent. of nitrogen, in a sample taken from the top of a filled cylinder at ordinary air temperature, would be difficult of accomplishment, as this would probably entail an average purity all through the cylinder of nearly 99 per cent. nitrous oxide.

Dr. PARKINSON referred to Dr. Hadfield's account of the unsatisfactory anæsthesia obtained by Dr. Phillips in three consecutive cases from a single cylinder of gas. He expressed regret that the exhaustive chemical analysis of the residue of gas remaining in the cylinder should have revealed so little to account for the untoward symptoms. Apparently the only impurity present was nitrogen and this was present to the extent of about 3 per cent. He reminded the meeting that this could hardly have accounted for the symptoms since air normally contains 79 per cent. of this gas.

He briefly described the procedure under the Foods and Drugs Act of "sampling" official drugs, explaining that an essential step was to divide the sample into parts, returning

one to the vendor for his own private analysis and to support his defence. He pointed out the difficulties of applying any such rules to liquefied nitrous oxide.

He further put forward the suggestion that in order to obtain a representative sample of the contents of the cylinder, it would be necessary to empty the same completely into a small gas holder and remove a sample therefrom, after having allowed time for diffusion of all the gases to take place. He agreed, however, that there was some argument against this and in favour of analysing the gas drawn directly from the cylinder, since this was the usual way in which it was used by the anaesthetist.

Postscript by Dr. Parkinson.—Later in the discussion the point was raised that nitrogen present as an impurity existed in one or more of the following states:—

(1) In a gaseous condition, floating at the top of the liquid nitrous oxide in the cylinder, in which case it would be entirely discharged when first the valve was opened. (2) In solution in the liquid nitrous oxide. (3) Actually liquefied and inseparably mixed with the nitrous oxide.

The last state was considered most improbable in view of the known difficulty of liquefying nitrogen, the second event was thought to occur possibly to some extent, but the first stated occurrence was considered most probable. Arising out of these points Dr. Parkinson explained that, as far as one firm at least was concerned, all such nitrogen would be blown off as a routine procedure before the cylinder left the factory.

Mr. H. E. G. BOYLE said that as he understood what had been said it appeared that the first lot of gas drawn from the cylinder might contain an extra quantity of nitrogen, that the gas drawn off from the liquid would contain less nitrogen, but this did not seem to fit in with the account that Dr. Ramsey Phillips had given of his cases, for here not only was the patient in the first case very ill after the administration, but other patients to whom gas had been given from the same cylinder were also affected. How could this be explained?

Dr. HAROLD KING said that, although all the previous cylinders of gas examined by him appeared to contain no impurities of note, within the last few days a cylinder of nitrous oxide had been received which undoubtedly contained higher oxides of nitrogen. The gas reduced permanganate and set free iodine from potassium iodide and starch. He also regarded as valueless the ferrous sulphate test for nitric oxide as an impurity in nitrous oxide.

Dr. J. MAUGHAN said that Dr. Hadfield had produced an able paper on what was admittedly a most difficult subject. In answer to the question of the clinical signs observed during the administration of the faulty gas, he said that there was a definite and progressive failure in circulation as from the tenth second. He would remind the Section that the average age of the three patients presenting the strange anomaly was 8 years. Mr. Boyle's two cases reported in the *British Journal of Anaesthesia* were interesting because brandy effected a recovery in each case, thus suggesting a condition of vagotonia amenable to alcohol. Dr. Dudley Buxton, in commenting on these two cases, was of opinion that the explanation lay in acute dilatation of the heart. The question might, however, be asked: What was the cause of this sudden dilatation during a nitrous oxide anaesthesia? He (Dr. Maughan) added that this was the first time in his experience of over forty years that three consecutive cases reacted to N_2O in the same abnormal manner. He felt it his duty in the circumstances to report the facts to the Section.

Dr. W. J. MCCARDIE said that he had received complaints from dental surgeons that occasionally they had experienced cases of collapse during and after nitrous oxide anaesthesia. He had himself inhaled the remainder from the cylinders used and had not found any alteration in the quality of the gas, and had also administered some of the gas without noting any special effect. He thought that the grave symptoms were due to asphyxia or acute dilatation of the heart, sometimes combined with the effect of fear. Nearly all the cases of collapse he had heard of or read of in this country, or which happened in his experience, occurred during administration for dental work, i.e., when the patient was sitting upright and when operation was done in the mouth. He had not known of any case in this country, except one of his own, in which the patient collapsed during prolonged surgical operation under gas, or gas and oxygen, although Baldwin had recorded many deaths in America occurring in major surgical work. Baldwin did not attribute these deaths to impurity of nitrous oxide.

He (Dr. McCardie) could not say that he had ever, in more than twenty-seven years' experience, met with cases at the Birmingham Dental Hospital or in private work in which he attributed ill effects to impure nitrous oxide, and he believed that the manufacturers supplied as pure a "gas" as was possible.

Section of Anæsthetics.

President—Dr. F. E. SHIPWAY.

Anæsthesia in Relation to Disturbances of the Circulation.

By C. E. LAKIN, M.D.

ONE hears it stated with increasing frequency that if there is doubt as to whether a patient is in a fit condition to stand an anæsthetic, it is the anæsthetist and not the physician who should express that opinion. I feel, therefore, that no mean compliment is being paid to the branch of medicine which I represent by asking me, a general physician, to address you this evening. If I may define the limits of this paper, I would say that the question of anæsthesia in Graves' disease has recently been so ably expounded before this Section by Dr. Strickland Goodall, that I do not propose to touch upon this subject, nor do I intend to say anything about spinal anæsthesia, as my experience is too limited to enable me to express any critical estimate of its use in cardiac conditions.

In a well-known text-book, written by a distinguished American anæsthetist, there is a statement with which I would join issue at the very outset. He is discussing the suitability of cases for anæsthesia, and the statement in question reads, "Unless some definite signs such as swollen ankles, pulmonary œdema or dyspnoea are present it is unnecessary to pay attention to any heart lesion." On those occasions in which it has been my melancholy duty to perform a necropsy on persons who have died during anæsthesia, these manifestations of loss of compensation referred to by the American author have not usually been present during life, and yet in a number of these cases clear signs of myocardial degeneration have been detected in the post-mortem room. Now the existence of *valvular* disease of the heart is manifested by definite clinical signs and is not likely to be overlooked, nor is it frequent for persons suffering from this condition to succumb under anæsthesia, but are there any means of recognizing cases in which definite *myocardial* change prevails? In studying departures from the normal we are apt to lay stress upon the more striking abnormalities and neglect less obvious aberrations. The student, therefore, interests himself in adventitious murmurs, and where these are absent gives scant attention to alterations in the character of the heart sounds themselves. Yet it is by the study of the character and rhythm of the heart *sounds* that the recognition of serious forms of myocardial degeneration becomes possible. The first sound of the heart is the result of two component factors, viz: the contraction of the ventricular muscle and the vibration set up by the closure of the auriculo-ventricular valves. In the healthy heart the first sound is low-pitched, dull and booming, as compared with the second sound, which is sharper and shorter. Where myocardial degeneration has taken place the first sound loses its low-pitched, booming, muscular character, and becomes shorter and higher pitched, like the second. Moreover, whereas in health the second sound follows the first after a short interval, and in turn is succeeded by a long pause before the next first sound is heard, in myocardial degeneration these periods of silence become approximately equal in duration, and the rhythm resembles that of a ticking watch. When, therefore, in the course of our examination we find that the first

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sound of the heart has lost its muscular character and has become sharp and short and perhaps weak, and that the pauses between the sounds are equal in duration, we are justified in drawing the conclusion that the muscular power of the heart is in abeyance, due either to a lack of tone or to definite and serious degeneration. At this stage there need be no cardiac dilatation. It is only when dilatation supervenes that we are likely to find cardiac irregularity, palpitation and dyspnoea. Extreme fatty change, for example, may be present, as in pernicious anæmia, and yet the pulse may be full and regular, and there may be a complete absence of signs of cedema of the feet or of the lungs. With the onset of dilatation a systolic murmur may appear at the apex and sometimes a gallop rhythm develops. In both fibroid and fatty change, as the condition progresses, the patient may awake in the early morning in an attack of cardiac asthma, or may show Cheyne-Stokes respiration, or he may awake feeling faint and nauseated, or may actually sit up in bed and vomit. Syncopal attacks and sudden death may follow exertion or a big meal. In the majority of cases degenerative changes are present in the aorta and frequently in the coronary arteries, and the patients have attained middle age or are elderly. The blood-pressure is frequently low and thus bears witness to the enfeebled state of the myocardium. If one uses a differential stethoscope, instead of the intensity of the first sound at the apex bearing a 2 to 1 relation to the intensity of the aortic second sound at the base, it approaches 1 to 1.

To recapitulate, if, in a middle-aged or elderly patient, one finds a tic-tac rhythm with the first sound resembling the second in character, a low blood-pressure and a ratio of 1 to 1 when a differential stethoscope is used, even in the absence of any cardiac enlargement or of any irregularity of the pulse or any of the ordinary signs of loss of compensation, one is justified in regarding the condition as that of myocardial degeneration. Such hearts appear to be unduly prone to ventricular fibrillation (though I know that the very opposite view has of recent years been gaining ground), and it is probably on this account that chloroform anæsthesia has frequently been attended by disaster. Even if all goes well at the time of operation, chloroform after prolonged anæsthesia produces a toxic, depressant action on the heart quite distinct from its direct action during the stage of induction, and this is sometimes responsible for more prolonged cardiac failure which may terminate in death. It will thus be seen how important it is in cases of this sort to make inquiry as to the occurrence of feelings of faintness or any untoward attacks of dyspnoea or cardiac asthma, and where a history of such is elicited to give adequate consideration to the problem presented.

A tic-tac rhythm and shortened first sound of the heart has not always this serious prognostication. It is seen, for instance, in young anæmic women in whom an impoverished blood-supply to the heart has induced slight fatty change with a loss of tone rather than profound degeneration. As far as my experience goes, such persons are not bad subjects for general anæsthesia, though, where time permits, it may be wise to defer operation upon them till the condition of the blood has improved. Special care has to be exercised in the case of children and adolescents with a history of acute rheumatism if the first sound of the heart at the apex is so soft as to be almost inaudible. This occurs only in the most severe type of myocarditis and must be regarded as indicating imminent failure of ventricular contractility. Weak heart sounds occur also in status lymphaticus and chloroform will be avoided in all suspected cases.

Among patients suffering from myocardial degeneration a group can be recognized in whom a regular alternation in the force of the ventricular contraction can be distinguished. Such persons are said to show a pulsus alternans, that is, every alternate beat is smaller than the one which precedes it. In many cases the difference in the size of the pulsations as felt at the wrist are too slight to be detected by the finger, though they are well seen in a polygraph tracing. It is

possible, however, to detect such cases with a sphygmomanometer. It will be found, in determining the systolic pressure, that, when the pressure in the pneumatic arm-let is released, and the pulse just becomes perceptible at the wrist, in cases of *pulsus alternans* the pulse-rate becomes only half what it was at the outset; in other words, only the bigger alternate waves are coming through; with a further release of pressure every beat comes through and the pulse-rate returns to its previous level. The phenomenon of alternation of the pulse is usually indicative of a severe grade of myocardial degeneration, and cardiologists are in the habit of giving a very grave prognosis; for myself, I think, often too gloomy a forecast. I have come across two cases in which a patient's friends were told that six months' duration of life was all that could be expected; in one instance the patient is still walking about the streets engaged in the fatiguing pursuit of doing her daily shopping long after the time at which she ought to have expired; the other is not in such a fair state of health, though he is able to get about and do a limited amount of work. I am sure that only operations of urgency are justified in the case of such patients, and it will be interesting to hear if any Members of this Section have experienced difficulties in anæsthetizing such persons. Rest in bed for two or three weeks, if the circumstances of the case should allow, together with the exhibition of some drug like diuretin to improve the coronary circulation, would probably be the best preparation for anæsthesia in such cases.

Pulsus alternans, with its alternating small and large pulse waves, must not be confused with *pulsus bigeminus*, in which the pulse waves occur in pairs separated by a pause. *Pulsus alternans* is usually regarded as a sign of failing contractility of the ventricle, whereas *pulsus bigeminus* is often attributed to increased irritability of the myocardium and in these cases is not in itself of serious import. But a word of warning is necessary, for although *pulsus bigeminus* is frequently due to an extra-systole replacing each third rhythmic beat (the extra-systole being appreciable at the apex though it does not reach the wrist), yet it is sometimes attributable to heart-block, each third ventricular contraction being lost. Such cases should be further investigated and electro-cardiographic tracings taken.

Heart-block is another expression of myocardial degeneration requiring passing reference. The condition in its complete form may be recognized by a slow pulse-rate of 36 or under, the rhythm of which is generally quite regular, and by the possible presence of rapid pulsation in the jugular veins. In many cases epileptiform seizures—the so-called Stokes-Adams syndrome—occur, though this is more common during the time that complete heart-block is becoming established. Since deep chloroform anæsthesia not infrequently produces heart-block in animals, the ventricle assuming a rhythm entirely independent of that of the auricles, when a physician is consulted he usually says that chloroform should be avoided. It is only fair to state, however, that there are cases of heart-block on record which have undergone chloroform narcosis without mishap; but this is not saying that the use of chloroform is unattended with grave risk.

A slow pulse does not necessarily indicate heart-block. A trained athlete will frequently show a slow pulse, the rate of which is likely to double suddenly when he starts vigorous exertion. Exercise in cases of heart-block, on the other hand, produces little if any acceleration.

Children showing irregularity of the pulse due to sinus arrhythmia differ in no respect from other children in their response to anæsthetics. Nor need the presence of extra-systoles, if this is the only anomaly found on examination of the patient, give rise to any misgiving on the part of the anæsthetist. Auricular fibrillation, on the other hand, recognized by utterly disordered cardiac action and gross irregularity of the pulse, is evidence of cardiac failure. Should operation be imperative in cases of this sort and time allow, complete rest in bed for a week or two, with the exhibition of suitable doses of digitalis, may lead to such a dramatic improvement

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that the anæsthetist who had refused to take the responsibility of inducing anæsthesia by general means may feel that he is justified in inducing it. Only operations of the utmost urgency should be undertaken in these cases without preliminary treatment by rest.

The importance of seeing the patient a day or two before that on which he is to be anæsthetized in order that an examination, more especially of the cardio-respiratory system, may be made, need not be stressed at a meeting of London anæsthetists. Due notice is taken of the position which the patient naturally assumes and in which he breathes most easily. If it is found that he can only breathe comfortably in a propped-up position, or when lying on one side, the reason for this must be ascertained. At this preliminary examination certain simple tests can be carried out. The patient should be asked to take a deep breath and hold it; if he is unable to do this for thirty seconds it is probable that he has some cardio-vascular defect.

The effect of exercise on the pulse-rate should be noticed. The healthy heart responds by a gradual increase in rate and quickly settles down to normal when exercise ceases. A heart with poor reserve power shows undue acceleration of pace and only slowly returns to normal, the chief exception to this rule being seen in cases of heart-block where exercise rarely causes any quickening of the beat. The effect of exercise on the pulse pressure can also be observed. Pulse pressure is obtained by noting the difference between systolic and diastolic pressure. In a normal person exertion causes a rise in both the systolic and diastolic readings, but as the diastolic rises less than the systolic it follows that the pulse pressure is increased. A fall in pulse pressure implies a poor response to strain on the part of the cardio-vascular mechanism. If the patient is too ill to walk round the room, there is yet another test that may be of service: the systolic pressure taken in the supine position may be compared with the systolic pressure taken when the patient sits upright or stands. Standing should cause a slight rise of pressure; if the pressure falls, cardio-vascular inefficiency may be suspected and a more elaborate examination of the heart should be decided upon.

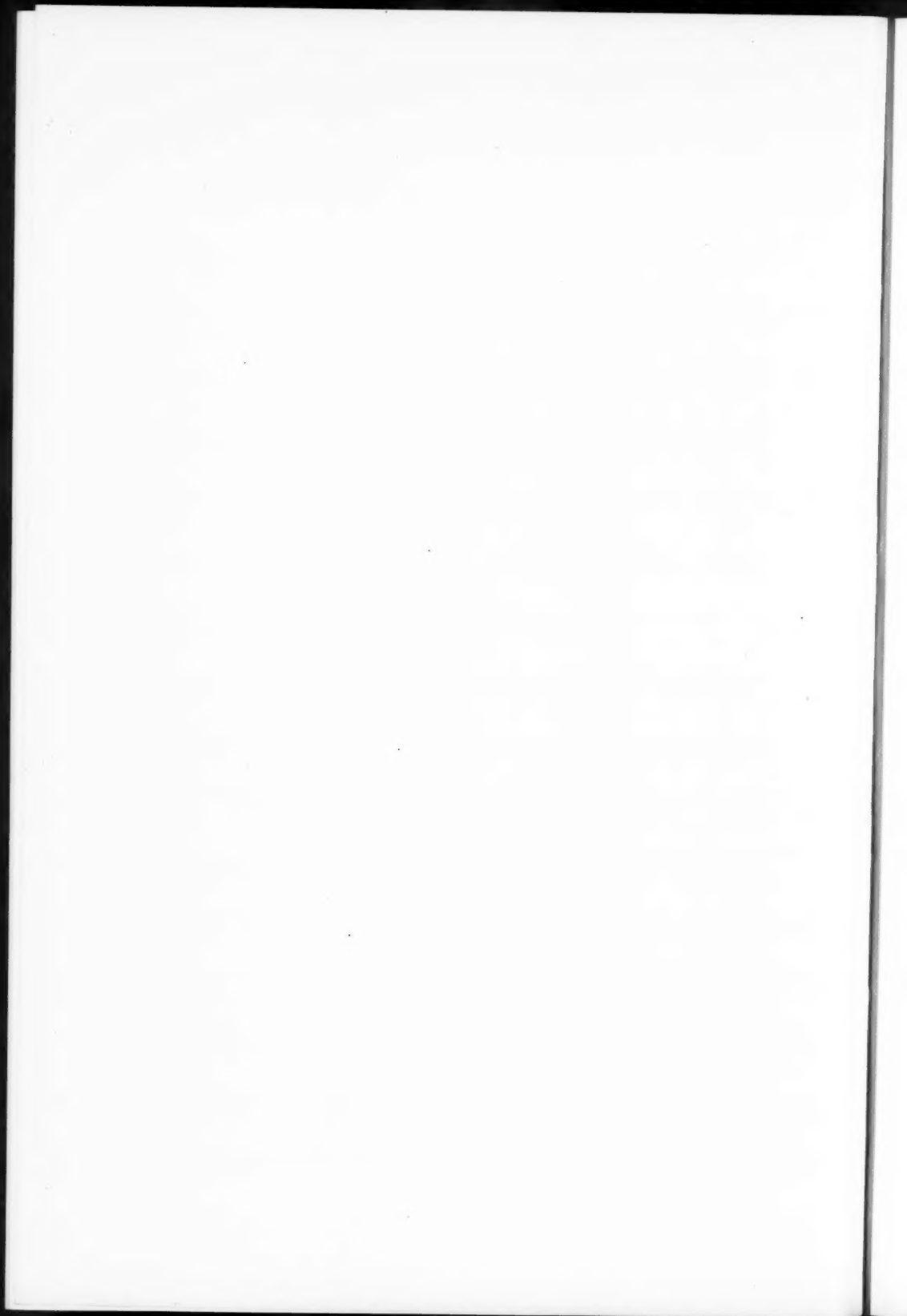
Operations under general anæsthesia in patients suffering from very high blood-pressure have sometimes proved disastrous. I remember a case in which a pontine hæmorrhage occurred during the course of the operation and the patient never regained consciousness. In all cases in which the systolic pressure is high, the diastolic pressure should always be taken. Diastolic pressure supplies us with a measure of the patient's peripheral resistance. Where this is only in the region of 90 mm., it is possible, if the patient is kept in bed for a week and given a saline purgative and iodides daily, to reduce the systolic pressure by 15 to 20 mm. of mercury. If, however, the diastolic pressure is raised as well as the systolic, the outlook is more serious, for the patient has arterio-sclerosis and probably interstitial changes in the kidney, and it will usually be wise to have a careful test of renal efficiency undertaken lest uræmia supervene upon anæsthesia. Anæsthetics such as ether or nitrous oxide and oxygen, which tend to raise blood-pressure, should be avoided.

When we come to consider the opposite condition, it has been my experience that persons with unusually low blood-pressure are liable to be much upset by morphia, and I hold that its use before operation in these cases should not be a routine practice. As blood-pressure falls during chloroform anæsthesia, chloroform should be avoided in this condition.

Time will not allow me to speak of the various devices and combinations which enable an anæsthetist to give a minimum amount of volatile anæsthetic, nor is a physician in a position to state more than general advice in this direction. The anæsthetist himself is far better qualified to appraise the effects of the various means at his command.

Our American friends have provided us with certain rules of thumb and short-cuts to knowledge in the way of various indexes of operability and shock obtained by arithmetical manipulations of blood-pressure readings, and hæmoglobin and corpuscular determinations. But to a non-mathematical mind like my own, useful as these may be to others, they but serve to confuse the issue, and if I am asked whether a person is in a fit condition for an anæsthetic, I prefer to go back to those primary considerations which I have tried to set forth in this paper.

Mr. A. L. FLEMMING said he agreed with Dr. Lakin's suggestion that morphia was capable of producing a condition of collapse in certain subjects, as the late Sir Frederic Hewitt observed many years ago. He (Mr. Flemming) had abandoned the use of morphia as a routine preliminary narcotic, and he had met with instances in which patients suffering from post-operative shock, with presumably low blood-pressure, had collapsed or become more shocked after the exhibition of morphia. He (Mr. Flemming) asked whether the Trendelenburg posture was likely to be a source of danger in the presence of any particular cardiac lesion. (The reply: Probably not, if change of posture was brought about slowly.) He also asked whether blood-letting would be permissible in a subject of hyperpiesia of such degree as to make general anæsthesia dangerous. (The reply was in the affirmative.)



Section of Anæsthetics.

President—Dr. F. E. SHIPWAY.

SPECIAL SESSION WITH CANADIAN AND AMERICAN ANÆSTHETISTS.

Dr. F. E. SHIPWAY (President) offered the visitors to the meetings the most cordial and hearty welcome. The last occasion when members of the speciality in the two countries met was at the International Congress of Medicine in 1913. Members of the Section also took this visit as a great compliment to themselves, because it was fully realized that it was American workers who discovered general anæsthesia, one of the greatest boons ever conferred on humanity.

After a brief survey of the history of anæsthetics, Dr. Shipway said that he felt that the United States had great traditions to live up to in anæsthesia, and he could not help thinking that by their presence here, the American anæsthetists showed they were conscious of the debt they owed to their forerunners in the past, and that they were anxious to live up to the high standard which had been set them.

Some Bearings of the Physiology of Respiration on the Administration of Anæsthetics.

By J. S. HALDANE, M.D., F.R.S.

AN anæsthetic acting centrally on the whole nervous system does not merely produce anæsthesia, but also some degree of interference with the action of various stimuli concerned in the regulation of essential physiological processes; and unless these effects are avoided they may be harmful or even dangerous. I wish to speak first of harm which may result through interference with the normal regulation of respiration.

When an anæsthetic is pushed the lips of the patient are apt to lose their bright red colour, and may become definitely bluish, though there is no cessation or marked diminution of breathing. This change of colour indicates that the blood is not being fully oxygenated in the lungs, and in an animal one can see that the blood in the arteries has an abnormal bluish tinge. Another symptom of defective oxygenation is periodic breathing [1]. What, now, is the cause of the defective oxygenation? A few years ago I should have been content with the explanation that owing to the respiratory centre being less sensitive than under normal conditions to the stimulus of CO_2 , or, speaking more exactly, of rise in the hydrogen-ion concentration in the arterial blood, the alveolar air comes to contain less oxygen and more CO_2 than usual, with the consequence that the blood leaving the lungs is less fully oxygenated than usual.

This explanation, standing by itself, is, however, far from satisfactory. When, without time being given for gradual acclimatization, persons are exposed to air in which there is a simple deficiency in the oxygen percentage, or a corresponding deficiency in the barometric pressure, blueness of the lips and other symptoms due to want of oxygen are produced, although the oxygen percentage of the mixed alveolar air, as determined by actual analysis, is still so high that blood saturated with this air at the existing barometric pressure would not show any appreciable blueness or deficiency in its saturation with oxygen. This and many other facts led to the conclusion, first expressed in a paper by Meakins, Priestley and myself, in 1918 [2], that alveolar air as obtained for analysis represents only the *average* of what is present in thousands of alveoli. We can at once explain the anomalous facts just referred to if we assume that the oxygen percentages in different alveoli vary considerably. Those alveoli which have a higher oxygen percentage than the average will not be able to saturate the hæmoglobin to an appreciably higher extent with oxygen than the alveoli with an average oxygen percentage. On the other hand, those alveoli with a considerably lower oxygen percentage than normal may be unable to saturate the blood to anything beyond a

considerably lower extent than normal. The inevitable result is that when the depth of breathing is abnormally diminished or there is less oxygen than usual in the inspired air, the mixed arterial blood is less saturated with oxygen than usual, though the mixed alveolar air may have a normal oxygen percentage.

In order to appreciate this fact it is only necessary to look at a normal dissociation curve of the oxyhemoglobin of whole blood. On one side of the point on this curve, which corresponds to the oxygen pressure of normal alveolar air, there is what is almost a plateau, while on the other there is a declivity of increasing steepness. This is not the case as regards the dissociation of the bicarbonate which carries CO_2 in the blood. Hence irregular distribution of air in the alveoli does not interfere with the amount of CO_2 in the mixed arterial blood.

We showed experimentally that if, for any reason, the breathing is shallower than usual, even if at the same time it is much increased in frequency, so that the total volume of air breathed per minute is increased, symptoms of want of oxygen are produced. The shallow breathing has exaggerated the differences which are normally present in the oxygen percentages of different groups of alveoli, and has thus produced the abnormal symptoms. In order to produce periodic breathing—a sure sign of want of oxygen—in myself, I have only, while lying down in bed, to increase voluntarily my rate of breathing from its normal figure of seven to twenty. The shallower breaths with the increased rate are quite sufficient to produce the effect.

These considerations afford, I think, a satisfactory explanation of the ease with which deficient oxygenation of the arterial blood may be produced during anaesthesia. When pushed to the point of full anaesthesia, anaesthetics produce a diminution in the vigour of the responses to respiratory stimuli, and consequently a shallower type of breathing, leading naturally to abnormally diminished oxygenation of the blood. We are apt to feel satisfied if the breathing during anaesthesia shows no sign of stopping. We are consequently apt to attribute any such sign as slight blueness of the lips to defective heart-action rather than to defective breathing. I should like to draw attention to the importance of defective breathing in this connexion.

I now wish to emphasize the practical importance of maintaining the normal, or nearly normal degree of oxygenation of the arterial blood. When, in a healthy person, the degree of oxygenation of the arterial blood is kept for some time appreciably below normal, characteristic symptoms, consisting of nausea, headache and general depression, gradually appear, and last till long after the exposure to want of oxygen has terminated. These symptoms, when they are produced by exposure to diminished atmospheric pressure, are known as mountain sickness. Exactly similar symptoms are produced by the deficient oxygenation of carbon-monoxide poisoning, or of exposure to air in which there is a simple deficiency in the oxygen percentage.

The symptoms may not appear till after the exposure to want of oxygen has terminated; and not only they, but also other far more serious symptoms due to want of oxygen, may last for long after the exposure. Hence we must conclude that they are due to what may be called temporary damage of some kind to the tissues, and particularly the tissues of the central nervous system. By damage I do not necessarily mean gross structural damage which could be seen directly, but abnormal alterations of some kind in molecular structure.

There may be no immediate danger in such deficient oxygenation as exists during anaesthesia, but the after-effects may be most unpleasant, and even dangerous to a patient suffering severely in other ways. I think, therefore, that it is well worth while to consider how the defective oxygenation may be avoided. We can certainly do so by adding oxygen to the air breathed along with the anaesthetic; but except when nitrous oxide is being used oxygen is hardly needed for other purposes in anaesthetic practice. We can, however, easily avoid the defective oxygenation by adding a small amount of CO_2 to the inspired air. CO_2 is the natural stimulus to breathing. If we take care that there is a little more CO_2 than usual in the inspired air we can avoid the natural tendency to shallower breathing during anaesthesia. A sufficiency of CO_2 prevents the breathing from being abnormally shallow, and in this way abolishes the defective oxygenation produced in the manner just described.

The simplest method of ensuring an excess of CO_2 is merely to administer the anaesthetic in such a way that the patient re-breathes part of his own expired air. The advantages have quite recently been pointed out clearly by Dr. Shipway [3]. By this method the oxygen percentage of the inspired air is also reduced; but the reduction does not matter as much. The deficient oxygenation of the blood is produced, not by want of oxygen in the inspired air, but by shallow breathing which, since the lungs do not expand evenly at all parts, leads inevitably to deficient oxygenation of the mixed arterial blood. When the inspired air is not

merely deficient in oxygen, but also contains a corresponding excess of CO_2 , there is not the same tendency towards deficient oxygenation of the arterial blood before sufficient CO_2 is present to produce extreme panting.

A further point is also important. When deficient oxygenation by itself is present it is always also the case that the breathing is stimulated to some extent by want of oxygen. But the stimulus is an abnormal one, and leads, generally speaking, to increased rate rather than increased depth of breathing. Now mere increase in rate is relatively ineffective in relieving the defective oxygenation, but an abnormally large proportion of CO_2 is washed out of the blood, and this produces a state of alkalosis. The consequences of this alkalosis are very serious for the circulation. It appears to be the case that the maintenance of a proper blood-flow through any part of the body is dependent on the avoidance of alkalosis. When deficiency of CO_2 accompanies deficient oxygenation of the blood we observe the grey or violet-grey form of cyanosis. This means defective circulation as well as defective oxygenation, and is a much more serious condition than what may be called a full blue cyanosis.

The effect of CO_2 in rapidly relieving symptoms of want of oxygen in so far as they are caused by defective circulation due to alkalosis is, I think, very strikingly shown when an animal is reduced to a state of stupor and paralysis by breathing air containing about 0.2 or 0.3 per cent. of CO . On adding about 4 per cent. of CO_2 to the inspired air, without making any reduction whatever in the percentage of CO , the animal immediately brightens up and becomes more lively; and exactly the same result is produced if human expired air is substituted for ordinary pure air, with the percentage of CO unaltered. This improvement is in spite of the diminished percentage of oxygen in the expired air administered.

Thus by administering an anæsthetic, whether with a little CO_2 —say about 2 or 3 per cent.—added to the air breathed, or else by letting the patient re-breathe a good deal of his expired air, we prevent imperfect oxygenation of the arterial blood, and at the same time prevent the alkalosis which ordinarily accompanies it. It seems to me that physiological considerations point to its being well worth while to do this, with a view particularly to the patient's condition after recovery from the anæsthesia, particularly with anæsthesias of long duration.

I now wish to say something about the use of CO_2 in another direction, clearly pointed out recently by my friend Professor Yandell Henderson of Yale University and his co-worker Dr. Haggard [4]. For evident reasons it is desirable to be able to get an anæsthetic both into and out of the blood and tissues as rapidly as possible. By using CO_2 to stimulate the breathing we can immensely hasten both the absorption and elimination of an anæsthetic given through the lungs. Why is this? When an anæsthetic enters the lungs during ordinary quiet breathing not much of it can reach the deeper alveoli, since it is absorbed rapidly in those alveoli which it first meets. Thus, of the blood passing through the lungs only a small proportion meets with the anæsthetic in anything near the concentration on which it possesses in the inspired air. As a consequence the mixed arterial blood leaving the lungs is at first not saturated to anything like the concentration corresponding to the concentration in the inspired air.

It is very essential to understand this point thoroughly, and I may perhaps illustrate it from what is now known quite definitely with regard to the rate of absorption of carbon monoxide when it is present in moderate percentages in the inspired air. By examining drops of the blood colorimetrically, or in other ways, we can easily measure the rate at which carbon monoxide is being absorbed. Now it has been found that when a given percentage of carbon monoxide is present in the inspired air the rate at which it is absorbed varies at first almost directly as the volume of the air breathed per minute until this volume is very greatly increased. If, moreover, during quiet breathing, we take a sample of deep alveolar air (as obtained from the last part of a very deep expiration) we find that it contains hardly any carbon monoxide. The carbon monoxide has thus scarcely penetrated to the deep alveoli during quiet breathing, and we see at once why the rate of absorption is so much increased by increasing the volume of air breathed; for far more of the gas gets into the deep-seated alveoli constituting the great mass of the lungs.

It is exactly the same during the administration of any ordinary anæsthetic. Anæsthetics are all soluble to a great extent in blood, though they do not combine chemically with one of its constituents, as do carbon monoxide or oxygen or CO_2 . The general conditions are, however, otherwise the same, so that it follows inevitably that by increasing the volume of air breathed we increase enormously the rate at which the anæsthetic is absorbed. Conversely, during recovery from anæsthesia we increase enormously the rate at which the anæsthetic is removed from the body if we increase the volume of air breathed per minute.

It has long been a familiar fact that we can get a patient under more quickly by inducing him to breathe deeply. But forced breathing, whether voluntary or involuntary, carries with it all the disadvantages which arise from the fact that during forced breathing far too much CO_2 is removed from the blood, with the result that a state of alkalosis is induced, and a consequent upset of various functions, including local regulation of the circulation.

To increase the breathing in a natural manner, and without upsetting other functions, by far the best method is to make use of CO_2 , which is the natural stimulus to increased breathing, and which Henderson and Haggard have introduced for this purpose. There is, however, a further advantage, as they clearly point out, in employing this method; for we can, without undue delay in producing anaesthesia, reduce considerably the concentration of the anaesthetic in the inspired air, thus avoiding both the risks to the heart and nervous system of eventual overdosage, and the bad effects on the respiratory passages of a high concentration of the anaesthetic, where, as in the case of ether, these bad effects are of considerable importance. We can, in effect, ensure such a concentration of the anaesthetic as will produce effective anaesthesia without going beyond this concentration in efforts to get the patient under rapidly.

A certain amount of time is undoubtedly required to get the patient under, even when, owing to the action of CO_2 , the whole of the blood passing through the lungs is utilized almost evenly for getting the anaesthetic into the circulation. The delay is due to the fact that not only the blood, but also the tissues, must be saturated up to the required point with the anaesthetic. Before this point is reached the charged blood must return again and again to the tissues, discharging into them at each round of the circulation a diminishing proportion of the charge, till saturation is reached. At the same time the charge contained in the blood leaving the lungs must progressively increase till it corresponds with the full percentage of the anaesthetic in the inspired air. The conditions under which an anaesthetic is being absorbed differ from those under which extra nitrogen is being absorbed during exposure to compressed air. In the latter case the charge in the arterial blood is maximal from the start.

In this process it is chiefly the central nervous system that we have to think of. Our knowledge of the rate of circulation through different parts of the body is still very imperfect, but, as was pointed out several years ago by Douglas and myself, such knowledge as we possess points very strongly to the fact that the circulation through the central nervous system during rest in man is not only very rapid, but also very large, in comparison with the rate through other parts of the body. Thus the central nervous system, or at any rate its grey matter, will saturate itself up comparatively rapidly, and then almost cease to absorb more of the anaesthetic when its concentration in the inspired air is not too high. This circumstance is very fortunate, but it must be remembered that in long anaesthesias other parts of the body with a slower circulation will be saturating themselves up all the time, and after the anaesthesia will take a correspondingly long time to free themselves, and consequently to free the blood, of the anaesthetic.

In the process of freeing the body from the anaesthetic after it has done its work, increased breathing is just as important as in the administration of the anaesthetic. If the breathing is not increased the deeper-seated alveoli can do very little towards getting rid of the anaesthetic. Its elimination is therefore very slow. The increased breathing washes it out much more rapidly, since the whole of the internal lung-service is brought into effective operation.

The addition of CO_2 to the inspired air has the great advantage that it is an effective preventive of imperfect saturation of the arterial blood with oxygen, as well as an effective preventive of alkalosis. It ensures adequate ventilation of all the alveoli, without risk of alkalosis. In former times, before the physiology of regulation of the breathing was understood, the presence of even a very small percentage of CO_2 in the inspired air was regarded with suspicion. We now know, however, that even though as much as four or five per cent. of CO_2 be present in the inspired air this leads to only a very slight increase in the proportion of CO_2 in the alveolar air or blood. The increased breathing produced by the very smallest increase in the percentage of CO_2 in the alveolar air brings down this percentage to nearly normal.

As to the best apparatus for ensuring at the same time a sufficiency of CO_2 in the inspired air, and a sufficiency, but not excess, of anaesthetic, opinions are sure to differ, and practical experience can alone decide. It seems evident, however, that mere re-breathing cannot be satisfactory, on account of the difficulty in satisfactorily regulating either the percentage of anaesthetic or that of CO_2 . It seems to me that an apparatus which enables us to fix at will, and quite independently of one another, the percentages of CO_2 and of anaesthetic, is needed.

It costs practically nothing to produce a very large and constant supply of air containing, say, five per cent. of CO_2 , and to regulate the percentage down to three or less if desired. If the patient's air-supply is drawn from this stream, and passes through another apparatus which regulates the percentage of anæsthetic to whatever is considered a desirable amount, we have what is needed.

An apparatus, designed at my suggestion, for furnishing quite automatically a large stream of air containing a fixed percentage, not exceeding five, has been in use for some time in treating cases of gassing in mines, &c. [5]. Other forms of apparatus, the first of which, so far as I am aware, was that of the late Mr. Vernon Harcourt, exist for regulating automatically the percentage of anæsthetic to a definite amount. It seems to me that a combination of apparatus of this sort would be practicable, and would fulfil the conditions which I have just indicated. As soon as satisfactory anæsthesia was produced the percentage of CO_2 could be cut down, so as to prevent waste of anæsthetic, and reduce the respiratory effort.

It does not seem to me to be necessary to use oxygen except in the case of nitrous oxide or any other gas with similar anæsthetic effect, only produced when so large a percentage of the gas is needed as to diminish seriously the oxygen percentage in the inspired air. With nitrous oxide a mixture of the pure gas with pure oxygen, undiluted with air, seems to me to be necessary whenever operations exceeding about a minute in duration have to be undertaken. Without the oxygen a state of acute anoxæmia will be produced. This induces very rapid anæsthesia, but at a serious cost to the patient if the anoxæmia lasts more than a very short time.

So far as I am able to judge, the introduction by Yandell Henderson of the use of CO_2 as an adjuvant to anæsthetic administration constitutes a very great advance. The particular methods which I have suggested for administering it are slightly different from those which he discussed in his recent lecture recently delivered here under the auspices of the Dental Board of the United Kingdom. There are also some small differences in detail as regards the explanations I have suggested of how CO_2 acts in hastening the absorption and elimination of anæsthetics; and I have perhaps laid more emphasis than he has on the good effects of the CO_2 on the circulation. But as regards the use of CO_2 I am a whole-hearted disciple of his, and in concluding this paper I should like to recommend a careful perusal of his lecture to any of my audience who are not already familiar with it or with his and Dr. Haggard's previous writings on the subject.

REFERENCES.

- [1] DOUGLAS and HALDANE, *Journ. of Physiol.*, 1909, xxxviii, p. 401. [2] HALDANE, MEAKINS and PRIESTLEY, *Journ. of Physiol.*, 1919, lii, p. 433. [3] SHIPWAY, *Guy's Hospital Reports* January, 1926. [4] HENDERSON, *Brit. Med. Journ.*, December 19, 1925. [5] HALDANE, *Trans. Institution of Mining Engineers*, 1924, lxviii, p. 271.

Dr. S. R. WILSON (Manchester) said it had been a great satisfaction to him to hear a scientific explanation of phenomena which many anæsthetists had observed clinically for years. In his younger days he found that the only satisfactory way of overcoming difficulties of breathing and surgical shock was by the use of the old Clover inhaler; so much was this so that he named it the "shock-absorber." He found that even a trace of cyanosis was most detrimental, and it was not until the oxygen tube was added at the end of the Clover bag that a more satisfactory form of anæsthesia was produced. In anæsthesia any cyanosis, he considered, was unsound; but in laparotomy, while the lips and ears remained pink, the edges of the abdominal wound continued blue. This required explanation.

He had used CO_2 for two years, and with most satisfactory clinical results. But he thought the physiologists were a little autocratic in the way they suggested its use, ignoring the sensory reflexes which surrounded the upper air passages, and which only the practical experience of the anæsthetist could coax out of the way. If given CO_2 it was true the patient must breathe, but he need not do so until he was at or near the breaking-point. All methods implied some re-breathing, particularly for the elimination of the anæsthetic and to maintain the breathing when the surgeon was embarrassing it—for instance, in putting a bridge under the thorax when doing a gall-bladder operation, which reduced the respiration to about 40 per cent. of the normal—deep anæsthesia was required, and the physiologist said "Put in CO_2 ." Under deep anæsthesia the sensitiveness was dulled, and under these circumstances one had to seek the aid of oxygen. He asked that attention be given to the reflex and sensory sides.

Dr. WESLEY BOURNE said he was a little surprised to hear Professor Haldane refer to the alkalosis which might occur in anaesthesia. On the contrary he (the speaker) remembered there was always a so-called acidosis. Perhaps Professor Haldane had overlooked the depressant effect of all anaesthetics on the respiratory centre.

Dr. McMECHAN said that he was glad to hear Dr. Wilson emphasize the necessity of oxygen in conjunction with carbon dioxide. That lesson was brought home to him all the more from the fact that in the experiences of Major Schroeder, the aviator in the United States who attempted to set up a new altitude record—one could study all the phenomena of analgesia at 25,000 to 30,000 feet. Aviators found that with oxygen and a slight amount of deep breathing they met all the requirements of respiration. Clinically, he agreed with Dr. Wilson that, on the table, it was more frequently necessary to have oxygen at hand than it was to have carbon dioxide; the anaesthetist was more often asked to secure a "silent abdomen" than to increase either the rate or the depth of the respiration.

With regard to some work which has been done in America, from a different standpoint, by de Sajous, the eminent endocrinologist, who disagreed with the diffusion theory of the physiologists, that worker insisted that there was a basic phenomenon underlying the function of respiration involving the secretion of adrenalin. He contended that unless this were present in the blood-stream and was being actively secreted, it was very difficult for the rest of the physiology of respiration to occur. Corbett, at Minneapolis, had shown that in most of the acutely ill patients who were subjected to operation there was an almost complete annihilation of the reserve of adrenal secretion, and in such, even using carbon dioxide and oxygen, one was hard put to it to preserve the vital functions. Sajous seemed to have supplied material for thought in regard to these cases.

With regard to carbon dioxide, some anaesthetists, in their clinical work, attempted to use very high percentages of CO_2 , and its use in an apparatus in which the quantity could be "stepped up" was fraught with possible danger. The types of patients might be two: one consisting of those apt to be in a state of alkalosis before anaesthetization was begun, and in such cases the anaesthetist would be chary about increasing, by stimulation, that carbon dioxide. In that type, indeed, the respiratory function should rather be repressed before anaesthesia was begun.

And in discussing these matters it must be remembered that one part of the body might be in one condition, and another part in another. Excellent studies along these lines were being carried out by Peyton Rous, of the Rockefeller Institute. He had shown in experimental work that the adrenal cortex might be in a condition of alkalosis, and the medulla in a condition of acidosis, or *vice versa*.

Professor HALDANE (in reply) said that he agreed with Dr. Wilson that one must avoid anoxemia, but for that purpose he did not think oxygen was wanted at all under ordinary circumstances, as everything could be done with CO_2 . The blue tint of an abdominal wound interested him very much. Henderson showed, in his animal experiments on shock, that if the abdomen was opened and the intestines exposed, they became blue, though the breathing of the animal was proceeding well. Henderson found that this could be prevented at once by keeping the surface of the intestine in an atmosphere containing 5 per cent of CO_2 , or bathing with saline solution saturated with such air. He fully acknowledged the difficulties on the reflex side, but by manipulating the CO_2 and the anaesthetic together, he thought these difficulties could be got over.

He did not refer to Dr. Wesley Bourne's papers, as he had not them by him, but what that gentleman had shown was that in full ether anaesthesia there was a condition of acidosis as compared with normal standards in the blood. Yet there was not enough CO_2 to stimulate the respiratory centre properly. In the case of a patient in the first stage of an ague fit, the action of the toxin had altered the standard of heat regulation of the body from 98.6° to 104° F. suddenly, and the body behaved as if it were far too cold, and the circulation through the skin was diminished. He believed there was a state like that in anaesthesia, though by absolute standards there was acidosis. He would add something on that to his paper, as it was very important.

Addendum.—When a patient is deeply under the influence of an anaesthetic the natural tendency must be, since the respiratory centre is less sensitive to its normal stimulus of increase in hydrogen-ion concentration (due to increased partial pressure of CO_2), for the hydrogen-ion concentration and CO_2 pressure in the arterial blood to increase. That this increase of

hydrogen-ion concentration does actually occur in deep ether anæsthesia has been shown by an exact method (that of Dale and Evans) by Stehle, Bourne and Barbour,¹ as well as by other observers. Besides this increase of hydrogen-ion concentration, there is a very marked diminution in what Van Slyke called the "alkali reserve" of the blood. This diminution is, however, no evidence of increased hydrogen-ion concentration of the blood, since it occurs, as Henderson pointed out, when a state of acute alkalosis is produced by forced breathing. It is also an accompaniment of the alkalosis produced by the increased breathing caused by want of oxygen at high altitudes, in CO poisoning, &c. It seems to be produced by a purely mechanical process of equilibration of anions between blood and tissues, and may thus be caused by excessive removal of CO₂ from the blood, as well as by abnormal discharge of acid into the blood, as during very excessive muscular work, or in diabetic acidosis.²

The increased hydrogen-ion concentration in the blood and tissues during anæsthesia is, to my mind, an entirely natural and "laudable" change, to use an old-fashioned expression; but the probable interpretation of the diminished alkali reserve is that something different from the natural stimulus is helping to stimulate the breathing. In the incomplete or excitatory stage of ether anæsthesia this seems to be the stimulant action of ether itself; and to the risks following the relative alkalosis of this stage Yandell Henderson has repeatedly drawn attention. The experiments of Stehle, Bourne and Barbour show an actual alkalosis at first in ether anæsthesia. In the stage of deep anæsthesia I think that the progressive fall in the "alkali reserve" is due to the breathing being abnormally stimulated by want of oxygen—a very undesirable form of stimulation, as I have pointed out in my paper, and also carrying with it the consequences that when the anæsthetic is discontinued the breathing will be less ample than would otherwise be the case, and the anæsthetic will take longer to leave the body. We can avoid all these evil consequences by adding CO₂ to the air containing the anæsthetic, and I think that when CO₂ is used there will be found to be no deficiency in the alkaline reserve, though, of course, there will be the usual increase in the hydrogen-ion concentration of the blood, and this will be the full "laudable" increase.

I made no reference in my paper to intratracheal oxygen-ether anæsthesia. This was a revelation to me when I first saw it, in Dr. Mennell's hands, before the war. With this form of anæsthesia there can be no risk of imperfect saturation of the blood with oxygen, provided that the respiratory passages are clear; and Leonard Hill has shown that with the blood fully oxygenated the pathological symptoms usually accompanying apnœa are avoided. The interesting fact is that the patient can be kept in a state of apnœa during the whole operation. The explanation seems to be that the cardiac pulsations, communicated to the air in the lungs, are sufficient to drive enough of the oxygen mixture up and down between trachea and alveoli to keep the level of CO₂ in the arterial blood below the point at which it stimulates the respiratory centre. Mere diffusion would be much too slow to effect this. It would usually be a disadvantage to add CO₂ to the oxygen-ether mixture, as this would prevent the apnœa which, from the surgeon's point of view, is often so valuable.

Recent Investigations concerning Nitrous Oxide, and the Ignition Points of some Anæsthetic Vapours.

By J. BLOMFIELD, O.B.E., M.D.

WHEN the Council of the Section of Anæsthetics of the Royal Society of Medicine honoured me with an invitation to address its overseas visitors, my first concern was, naturally enough, to try to discover some work by others in connexion with our subject which was not already familiar to American and Canadian anæsthetists. Equally naturally this task was no easy one. The investigations and inquiries of our transatlantic colleagues, whether clinical or in the laboratory, and whether dealing with the physics, the chemistry, the biochemistry, or the physiology of anæsthesia, are widespread and incessant. It can readily be imagined, then, that I was much relieved at the suggestion that I should tell of the investigations of a certain Committee, which since it sits in London and has not yet reported, must be at present a sealed book, even to the indefatigable investigators of Canada and the United States. Indeed, it is not too much to hope that most of you have never even heard of this Committee, much less of anything that it may have achieved. To begin my story at

¹ Stehle, Bourne and Barbour, *Journ. of Biol. Chem.*, 1922, liii, p. 341.

² See the discussion in Chapter VIII of my book "Respiration," 1922.

its beginning, then, I must tell you that over two years ago a Committee, known as the Anæsthetics Committee, was jointly established by the Medical Research Council, which is a Government Body under the Privy Council, and the Anæsthetics Section of the Royal Society of Medicine. The Medical Research Council nominated Dr. H. H. Dale, now Secretary of the Royal Society, and Director of the National Institute for Medical Research, Professor Donnan, F.R.S., Professor of Chemistry at University College, London, and Professor Pembrey, F.R.S., Professor of Physiology at Guy's Hospital; and the Anæsthetic Section's Council appointed to serve with these distinguished men of science, Dr. F. E. Shipway, Dr. C. F. Hadfield and myself. The Committee has itself co-opted Professor Storm van Leeuwen, of the University of Leyden, as a corresponding member, and Professor H. B. Dixon, of Manchester University, who was already, on behalf of the Department of Mines, working at problems closely affiliated to some which arose from the deliberations of the Committee. Of these more will be said later. The formation of a joint committee of inquiry of this kind was first suggested by two factors : first, complaints as to abnormal effects of nitrous oxide in certain cases which from time to time reached the Anæsthetics Council, and secondly the fact that the "British Pharmacopœia" does not include nitrous oxide, and that therefore there were no official test of purity by which this anæsthetic is to be judged in this country. Although, however, it was this state of affairs, as regards nitrous oxide, which led the anæsthetists to approach the Medical Research Council, that body not only agreed at once to the formation of a Committee, but also desired that the inquiry should be much more general than one confined solely to laughing gas. Accordingly the investigations pursued include also the purity of ether, the use of acetylene, ethylene and propylene, and the ignition and explosion points of general anæsthetic gases either in combination with one another or with air or with oxygen. The practical importance of the last-mentioned inquiry is made evident by reports of fatal explosions in the course of anæsthesia that have taken place both in America, on the Continent, and in Great Britain. These explosions have occurred not only during the use of the newer and more explosive gases, acetylene, ethylene, &c., but also with ether, the inflammability of which has been lost sight of in some of the most modern methods of administering this anæsthetic.

The dealings of the Committee with nitrous oxide started by an inquiry into the cases reported by Mr. Ramsey Phillips, one of the anæsthetists to St. Mary's Hospital, who has very wide experience in the use of this anæsthetic in particular. This is worthy of mention because there is no doubt that in a vast number of complaints as to the misbehaviour of an anæsthetic it is the anæsthetist and not the anæsthetic who is responsible for the unusual symptoms observed. This is, I think, especially true of nitrous oxide, which being often given for dental work by those who have little experience, is held responsible for the occurrence of symptoms which are in reality due to want of knowledge on the part of the administrator, and, I may add, to want of air or oxygen on the part of the patient. Explanations of this kind are out of court when we are dealing with cases reported by experienced and highly competent anæsthetists and it is only to cases of that nature that I shall be referring.

Quoting Mr. Phillips' report, "six patients, four women and two men, were anæsthetized with the gas complained of. The gas used had a strong smell like brown potash or dirty wash-tub water. Clinically my complaint was that anæsthesia could not be produced without marked cyanosis; this led me to use the conjunctival reflex as a guide, a thing I never do in the ordinary way. This particular cyanosis was unusual. Lividity, white lips, grey colour of the skin, small to medium pupils, eyeballs looking directly forwards, and convulsions quite unlike the usual jactitation. In each case I gave large quantities of oxygen when this occurred, but the recovery was very slow. In some cases I had to re-apply the gas with free supply of oxygen, as I had not allowed the operation to be commenced. Exactly the same thing occurred. There was no observable obstruction to the air-way in any of the cases. On recovery, all the patients felt very poorly, pulse small, irregular and soft. Nos. 1 and 2 gave rise to considerable anxiety at the time. No. 3 felt really ill when there should have been no cause for it. No. 4 also. No. 5 was not a dental case, but was having her neck stretched and manipulated for an alleged dislocation, and the convulsions were put down by the surgeon to his manipulations, who felt rather pleased, I think. No. 6 was badly knocked out, but she was not a good subject for gas. I heard afterwards that she had had a severe cardiac breakdown after it. I have not met with this before or since. My apparatus was in good working order, and in each case there was plenty of oxygen in the oxygen bag at the end of the case. The clinical picture was quite different from the cyanosis and jactitation common in cases where most of the air is washed out of the lungs and no oxygen is given. Again there was the strong smell of the gas, and

the conjunctival reflex (taken well away from the cornea) was strongly present up to a point in some cases where I had to desist, and I was unable to say that the patient would not feel the operation. No cough or sign of irritation in the air passages was present, and no nausea followed. I rather naturally dreaded to go to another gas case. I went to the makers and told them about it. While assuring me that the gas was good and normal, they showed me how to smell and taste it, and produced other gas which they acknowledged had no smell, while that which I had been using smelt strongly. I changed my stock of gas, with the exception of the two bottles I sent you. While admitting that these difficulties may have been caused by myself, I felt it would be good to find out if the gas was good for human beings or not, since there are no regulations to control the manufacture."

The unused gas was sent to Dr. King—chemist to the National Institute for Medical Research at Hampstead. I should like to say here that the Committee is very greatly indebted to Dr. King for the prompt and able manner in which he has conducted many analyses dealing with nitrous oxide and also various ethers and other substances.

Dr. King reported as follows:—

"It was bubbled through silver nitrate solution. Absence of turbidity indicated *absence of halogens*.

Bubbled through dilute permanganate solution. No diminution of colour observed as compared with control, indicating *absence of reducing substances*.

Passed through dilute litmus solution made up in freshly boiled water. Solution rapidly became red as compared with control. *Acidic substances present*.

Passed through baryta solution. Rapidly became cloudy. *Presence of carbon dioxide confirming litmus test*.

Passed for a long period through ferrous sulphate solution. No darkening observed as compared with control. Hence, *absence of nitric oxide*.

Several qualitative tests showed that, on shaking small volumes, 5 to 10 c.c. with cold water in a eudiometer, there was always a small volume undissolved. Accordingly 500 c.c. of gas were collected over water in a large corked cylinder and shaken with successive portions of fresh water until no more was dissolved. The residual volume was about 12 c.c. This was transferred to a van Slyke gas analysis apparatus and, exposed to alkaline pyrogallol, showed no appreciable change of volume. *Absence of oxygen and carbon dioxide*. The residual gas was not inflammable and did not support combustion. *Absence of carbon monoxide and presence of nitrogen*.

Summary.—The nitrous oxide examined contained a small proportion of carbon dioxide and about 2 per cent of nitrogen."

A few days later Dr. Dale wrote as follows:—

"Since the last meeting, King and I have further examined the sample of nitrous oxide received from Ramsey Phillips. We passed the gas through a dilute solution of oxy-hæmoglobin until all the oxygen was blown out and reduction complete. The spectrum was then that of reduced hæmoglobin with only a single diffuse absorption band. This appears to me to exclude CO and NO beyond shadow of doubt and much more decisively than any animal test could, or any ordinary chemical test."¹

The details of this examination have been given both because the tests made and also the results obtained are closely paralleled by all the further investigations into samples of nitrous oxide of which complaint had been made. The noticeable fact is that in no instance was there found one of those formidable impurities, a halogen, nitric acid or carbon monoxide, to which at first sight one would naturally have attributed the unusual symptoms arising out of an inhalation of nitrous oxide in the hands of an expert administrator. The two impurities which alone figure at all frequently in the whole series of examinations are carbon dioxide and nitrogen. With regard to the first its presence has been in so small a quantity that it is hard to believe that it played any part in the production of symptoms. It was never present in as high a percentage even as that of normal alveolar air. The undue proportions of nitrogen require further consideration. In all cases that came before the Committee a variable percentage of nitrogen was found in the suspect gas. Among these cases was a series reported by the War Office through the Medical Research Council. The reports were similar to many others and had no feature of special clinical interest, but the gas concerned was exhaustively examined at the Government laboratory by Sir R. Robertson and his assistants and their full report was placed at our disposal. The percentage of nitrogen found in samples of the gas reached as high as 10 per cent. In many other instances we found 5 per cent. to 7 per cent.

¹ *Proceedings*, 1926, xix (Sect. Anæsth.), p. 20.

This nitrogen must be present in the cylinders in one of three states—either it must be dissolved in the liquid nitrous oxide, or it must itself be liquid, or it must be as a gas in the free space of the cylinder above the liquid nitrous oxide.

Now it does not seem likely that the admixture of a small percentage of nitrogen (say up to 5 per cent.) with nitrous oxide will have any very marked effect if that admixture is a reasonably even one. The nitrous oxide will, of course, be correspondingly weaker, but when we consider that nitrogen, by acting as an asphyxiant, would itself have a certain anæsthetic action, we should hardly expect it to be noticeably weaker. That is, of course, if it were given without much air or oxygen. The researches of Sir R. Robertson first directed the attention of the Committee to the fact that, especially with larger percentages, the admixture would not be an even one. Nitrous oxide, as we all know, is easily compressible, and becomes a liquid at a pressure of thirty atmospheres at 0° C. This fact has been largely used by the manufacturers as a test of purity. If their gas liquefies at the usual temperature and pressure, it is probably good gas. If it does not, the process has failed at some point and the gas has to be discarded. Nitrogen, on the other hand, is much less compressible and refuses to liquefy under the processes employed by the manufacturers. If, then, a sample of nitrous oxide containing a percentage of nitrogen is compressed into a cylinder, that cylinder will contain liquid nitrous oxide, while the space not actually occupied by the liquid will contain a high percentage of nitrogen in a gaseous condition. It is possible that a certain amount of the nitrogen would be actually dissolved in the nitrous oxide. As far as I can discover, we have no authoritative statement as to the solubility of nitrogen in liquid nitrous oxide. The point of practical importance is that when a cylinder containing such a mixture is opened, the composition of the gas first issuing from it will vary greatly according to the position in which the cylinder is held. If the cylinder is placed vertically with its mouth downwards (a position we anæsthetists never adopt), the gas should be pure nitrous oxide or nitrous oxide containing only such a proportion of nitrogen as is soluble in the liquid. If the position is reversed and the cylinder held upright with the mouth upwards, it will be the highly compressed but still gaseous nitrogen that will be tapped first, and the resulting gas will be nitrogen with a variable proportion only of nitrous oxide. With the cylinder held nearly horizontally the conditions will be much the same, but will vary according to the actual angle adopted. From this it will be readily understood that a cylinder of nitrous oxide containing an apparently harmless percentage of nitrogen may, under certain conditions, when first opened, yield a gas so rich in nitrogen as sensibly to affect its anæsthetic action. It is, in fact, probable that this relatively high percentage of nitrogen is the explanation of some of the abnormal symptoms that have been reported to us.¹

Among other reports which reached the Committee I may mention that concerning three children who were given nitrous oxide by an experienced anæsthetist at a school treatment clinic. All three showed signs of collapse without cyanosis. With the remaining patients treated from the same cylinder the anæsthetist gave only half or three-quarters of his usual amount and obtained good anæsthesia with normal recovery. The remaining gas was carefully examined, but was found chemically pure except that it contained some nitrogen. Professor Karsner, of the Lakeside Hospital, Cleveland, kindly supplied information relating to cases of poisoning by nitrous oxide in that hospital, which led to the installation of a complete plant for the manufacture of nitrous oxide in the hospital itself. That plan has not yet been adopted in this country and it does not seem necessary. The general purity of the gas supplied by the makers in Great Britain appears to the Committee to redound highly to their credit. Nevertheless it is obviously desirable that there should be a recognized official standard of purity for nitrous oxide and stated tests by which this can be determined, as indeed is already the custom in the United States of America and some other countries. With this recommendation in view the Committee are taking the view that samples of gas taken into the cylinder upright should contain at least 95 per cent. N_2O . In dealing with tests, Professors Donnan and Pembrey and Dr. Dale, with the help of Dr. Harold King, have taken the tests of the U. S. Pharmacopœia as a basis of the Committee's recommendations.

"Pass 2,000 mils of the gas, measured under normal atmospheric pressure at about 25° C., through 100 mils of barium hydroxide T.S. at a rate not exceeding 4,000 mils per hour; not more than a slight turbidity is produced (*carbon dioxide*).

¹ *Proceedings*, 1926, xix (Sect. Anæsth.), p. 22.

"No opalescence is produced in a mixture of 100 mls of distilled water and 1 mil of silver nitrate T.S. by 2,000 mls of the gas under the conditions described above (*halogens*).

"No change in colour is produced in 100 mls of distilled water, to which 5 drops of litmus T.S. have been added, by the passage of 1,000 mls of the gas through the liquid under the conditions described above (*acids or bases*).

"No alteration in colour is produced in a solution of 0.2 mil of tenth-normal potassium permanganate V.S. in 100 mls of distilled water by the passage of 1,000 mls of the gas through the liquid under the conditions described above (*reducing substances*)."

Of these tests the only one which fell under criticism, as possibly unnecessarily severe, was that for carbon dioxide, Professor Pembrey maintaining that the presence of a small percentage of carbon dioxide would be advantageous rather than deleterious. The tests do not provide adequately for the detection of nitric oxide, not specifically for nitrogen peroxide, and not at all for the detection of carbon monoxide.

For *nitrogen peroxide* Professor Donnan suggested that the following test should be adequate:—

The baryta solution used for detecting excess of CO_2 should subsequently be acidulated with sulphuric acid. A drop of dilute potassium permanganate solution added to this liquid should not be decolorized. (The test would need to be given in quantitative form, and carried out against a control in which an equal quantity of baryta solution, through which no gas had been passed, would be acidulated, and similarly tested with an equal addition of potassium permanganate.)

For *carbon monoxide* two tests came under consideration:—

(1) The hæmoglobin test, which has been used for the Committee.

It was agreed that further experiment would be needed before this test could be described in quantitative form and recommended for adoption. The available data show that not less than 0.07 per cent. of CO can be detected in *air* by the hæmoglobin test. In this case, however, the CO is competing for hæmoglobin against 20 per cent. of oxygen. It seems likely that much smaller proportions of CO in a gas indifferent to hæmoglobin, such as N_2O , could be detected by the production of spectral bands, permanent after the addition of a trace of sodium hydrosulphite, and therefore not due to oxygen. Such a test could be very easily carried out by anybody possessing a small direct-vision spectroscope. It would be necessary, however, to determine the limiting concentration of CO which can thus be detected.

Professor Pembrey undertook to make some mixtures of N_2O with small measured proportions of CO, and to determine the smallest concentration of CO which could thus be detected.

(2) *The Test using Iodine Pentoxide*.—This test is said to detect as little as 0.005 per cent. of CO, or, in other words, 1 c.c. of CO in 20 litres of gas. The gas is passed through a U-tube containing iodine pentoxide heated in a water bath to $60^\circ\text{--}70^\circ\text{C.}$, and the issuing gas is passed through a solution containing potassium iodide and starch. If a blue colour is produced the amount of iodine liberated can be determined with $\frac{1}{1000}$ N. sodium thiosulphate. It can be calculated that 1 c.c. of CO should liberate rather more than 2 mgm. of iodine, which would require about 25 c.c. of the thiosulphate solution. Two litres of gas, if containing 0.1 c.c. of CO, should therefore liberate an easily titratable quantity of iodine. This proportion of CO would be physiologically negligible, and the test, therefore, seems to be a perfectly efficient one. A blank control, in which the same volume of pure air was passed through the iodine pentoxide tube, would presumably serve as a preliminary. The test would be rather a cumbrous one for carrying out in an ordinary pharmacy.

Nitric Oxide.—It was thought probable that NO would react similarly to CO with the iodine pentoxide, in which case it would also be detected by the test above described. Members promised to obtain further information on this point, and Professor Donnan offered to have an experiment made. An alternative test suggested for NO was to mix the volume of gas to be tested with a suitable volume of air or oxygen, and, after allowing time for formation of NO_2 , to pass the mixture through a solution containing potassium iodide and starch, when any NO should be detected by the liberation of iodine. The test would, of course, also detect pre-formed NO_2 .

Test for Proportion of N_2O present.—The Committee's work has shown that the impurity most frequently responsible for trouble is nitrogen, which on compression will tend to occur, in higher than the general concentration, in the gas in the top of a cylinder

For the analysis of N_2O , Boothby and Sandiford's method (*Amer. Journ. Physiol.*, 1915, xxxvii, p. 377) is recommended—in which the 10-c.c. gas analysis apparatus is used. 2.5 c.c. of nitrous oxide is mixed with about 7.1 c.c. of hydrogen and burnt, and the contraction of volume noted. If the gas is freed from CO_2 and O_2 previously, the contraction gives the volume of N_2O in the original sample.

IGNITION POINTS OF ANÆSTHETICS.

The exact facts relating to the ignition of anæsthetic gases are obviously of great importance to the anæsthetist whose work is often carried out in proximity to the cautery or to the electric lamp of laryngoscopes and the like, if not to actually open flames. Nevertheless, these facts have not hitherto been clearly elucidated, and the general opinion has been widespread that as long as the anæsthetist avoided an open flame or a red-hot cautery his vapour could not be exploded. What must really be exploded is this opinion, for the researches of Professor Dixon have made it plain that a heat considerably less than that of a flame or that needed to make a metal red hot can ignite certain commonly used anæsthetic vapours. It was the ignorance of or the neglect of this fact that led to disastrous explosions on several clinical occasions. The researches to which I have referred were conducted in connexion with ether, ethylene, nitrous oxide and propylene.

There are three methods by which the problem has been attacked: (1) by bringing a mixture of the gases with oxygen or air into contact with a heated solid—generally the inner walls of a vessel, and noting the temperature at which the gas inflames; (2) by heating the gas and oxygen separately and then bringing them together; (3) by compressing the mixture of gas and oxygen adiabatically and observing the pressure necessary to fire it. In all these methods the time factor comes in.

The method employed with anæsthetic gases was that which Professor Dixon had used to determine the ignition points of methane and other gases for the Safety in Mines Research.

The apparatus consists of an upright silica cylinder, 2 ft. long and 5 in. wide, heated by an electric furnace which surrounds it. At the lower end of the cylinder, air, oxygen or other gas (such as nitrous oxide) is admitted at a measured rate, and is heated as it slowly passes up the cylinder, finally escaping at the top. In the axis of the furnace a narrow silica tube is fixed, opening with a 2 mm. orifice in the centre of the large cylinder. By the turn of a tap outside the gas to be ignited is admitted through this central tube and is heated to the same temperature as the atmosphere outside it before the gas and atmosphere have a chance of mingling. When the gas is turned on a small jet of gas escapes and comes in contact with the oxygen round it, a certain interval of time elapsing between first contact and ignition according to the temperature. This interval or "lag"—the duration of the pre-flame period—becomes less as the temperature of the furnace is raised, until finally it becomes half a second or less. The furnace is now allowed to cool slowly and the increasing "lags" are measured until the lag reaches ten seconds. The mean of the rising and falling temperatures registered respectively at half, one, two, three, five, seven and ten seconds' lag is taken as the ignition-point with that lag. The observations of the flame are made through a small window in the roof of the furnace.

The outer steel casing round the furnace allows the experiments to be made either at atmospheric pressure or above or below that pressure. For high pressures the cylinder is filled with oxygen from a steel bottle and the central tube is supplied from a bottle of the compressed gas.

The ignition-points of ethylene in oxygen vary with the pressure. At normal pressure the rapid ignition-point is $604^{\circ}C.$, a temperature at which a solid body is just visibly red in a dark room. But the gas will ignite at a lower temperature if contact between the heated gas and oxygen is maintained; such ignition occurs after one second at $593^{\circ}C.$, after two seconds at $584^{\circ}C.$ and so on until, if contact is maintained for ten seconds, the gas will ignite at $554^{\circ}C.$ The lowest temperature I have observed for the ignition of ethylene in oxygen at normal (atmospheric) pressure is $544^{\circ}C.$ after a lag of fifteen seconds.

When the pressure is raised above the normal the ignition-point of ethylene in oxygen falls slowly and nearly regularly, and in this it resembles other inflammable gases. For instance, at two atmospheres' pressure the gas ignited rapidly in oxygen at $580^{\circ}C.$, and at three atmospheres at $557^{\circ}C.$ The lowest ignition-point recorded was $501^{\circ}C.$ at three atmospheres' pressure after a lag of fifteen seconds.

When the presence of the oxygen is reduced the ignition-points rise until a maximum is reached at about half an atmosphere. From this point the ignition-points fall rapidly as the

pressure is reduced to 100 mm. of mercury, but at this low pressure the gas does not ignite after three seconds' lag.

In the following table the mean ignition-points of ethylene in oxygen at different pressures are recorded with the several pre-flame intervals or "lags":—

Lag seconds	100 mm. degrees	250 mm. degrees	400 mm. degrees	760 mm. degrees	2 Ats. degrees	3 Ats. degrees	4 Ats. degrees
5 ...	594 ...	650 ...	660 ...	604 ...	580 ...	557 ...	535 ...
1 ...	581 ...	634 ...	646 ...	593 ...	572 ...	549 ...	—
2 ...	563 ...	614 ...	625 ...	584 ...	562 ...	538 ...	—
3 ...	555 ...	597 ...	606 ...	577 ...	554 ...	530 ...	—
5 ...	—	585 ...	590 ...	569 ...	546 ...	523 ...	—
7 ...	—	574 ...	578 ...	561 ...	540 ...	515 ...	—
10 ...	—	563 ...	567 ...	554 ...	532 ...	508 ...	—
15 ...	—	—	—	544 ...	525 ...	501 ...	—

Experiments in the ignition of propylene in oxygen were carried out in the same manner as those for ethylene. The gas was caused to issue through a narrow central tube, with 2 mm. orifices in the centre of a large cylinder fed with a stream of oxygen from below. The cylinder heated by an electric furnace is packed in a strong steel case so that the pressure of oxygen may be varied. The heated oxygen is continually drawn off from the top of the furnace so that the atmosphere round the central tube is constantly renewed with fresh oxygen. After each ignition the products of combustion are drawn away with the excess of oxygen, and time is allowed for the central jet to cool down after the flame is extinguished. Propylene for these experiments was obtained from three sources:—

(1) Prepared and compressed in steel bottles by a private firm.
(2) Prepared in Professor Dixon's laboratory by passing iso-propyl alcohol over P_2O_5 in an iron tube.

(3) Prepared in the same way from normal propyl alcohol.

As the first portion coming from the bottle appeared to ignite at a lower temperature than the later portions Professor Dixon prepared samples of the gas from isopropyl and from normal propyl alcohol, passing the vapors over heated P_2O_5 on pumice in an iron tube at temperatures varying from 260° to 340° C. In each experiment some of the alcohol came through undecomposed and was collected in a condenser kept well cooled with ice and salt, and in each case a second liquid was collected. This liquid boiled between 82° and 83° C. and was an ether; its boiling point corresponds with that of mixed propyl-isopropyl ether. The propylene which was thus collected had practically the same ignition point as the later portions of the gas from the steel bottles. The propylene when tested in the concentric tube apparatus was found to behave like ethylene towards oxygen, i.e., the ignition point rose when the pressure was decreased and reached a maximum at about half an atmosphere's pressure. From this point the ignition temperature fell until at 50 mm. pressure the propylene lit at the same temperature as at the normal atmospheric pressure of 760 mm.

The ignition points found for propylene were all lower than that of ethylene, the difference being greatest at the maximum ignition point under 400 mm. pressure. The lowest ignition for propylene in oxygen occurred with 400 mm. pressure after a lag of twenty-five seconds, viz., 515° C. When propylene is heated in an atmosphere of air, higher temperatures are needed for ignition, the ignition point at normal pressure being 618° C. In air the maximum is found near 300 mm. pressure, 663° C.

Experiments which have been begun in an atmosphere of nitrous oxide show that the ignition points of ethylene and of propylene are lower in that gas than in oxygen.

Ether, Professor Dixon found to give curious results with his concentric tube apparatus. "You may get, he says, a low ignition with a short 'lag,' e.g., 220° to 260° C., and then as the temperature is raised the 'lag' increases until the vapour refuses to light at all; when the temperature is raised to 500° or 600° C. ignition again begins and the 'lag' shortens. Obviously the vapour is decomposed in the narrow silica tube, and if the gas is collected, after passing through, it is found to consist mainly of methane, ethylene, hydrogen and carbon monoxide."

These experiments point to two possible dangers in practice which would not, I think, have occurred to the minds of most practising anæsthetists, viz., that the risk of inflammability with ethylene, acetylene and propylene is increased by using them under pressure, and that it is increased if they are used in conjunction with nitrous oxide gas—the latter fact is, I think,

especially surprising as one would naturally have expected the inflammability to have been greatest when the anæsthetic was used, as it generally is, in conjunction with large proportions of oxygen.

In conclusion, with regard to the Committee's work on ether. This is still in progress and therefore no final statement can be made, but one important conclusion seems already pretty certain, viz., that ether is really an anæsthetic and the purer the ether the better the anæsthetic. This is at variance with the findings of some investigators, particularly Cotton across the Atlantic and Mackenzie Wallis in this country, who have appeared to find only in the impurities of ether its sources of narcosis. Formidable among these impurities are the peroxides. With regard to these, Mr. Henry King has supplied the Committee with this summary:—

Historical.—Schönbein, in 1851, first showed that an oxidizing substance was present in ether which had been exposed to the action of air and light. This has been confirmed by numerous other observers since, although its exact nature has only been discovered during the past year by Wieland and Winger (*Annalen*, 1923, 431, p. 301). Previously the oxidizing properties were attributed to a variety of substances such as ozone (Schönbein), hydrogen peroxide (Richardson), acetic peroxide (Nef), ethyl peroxide ($C_2H_5)_2O_2$ (Berthelot), and ethoxyethyl hydrogen peroxide (Clowes).

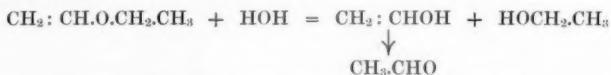
Wieland and Winger found that hydrogen peroxide and acetaldehyde react with production of dihydroxyethyl peroxide—



and this substance was shown to be identical with the oxidizing substance found in ether. Its formation from ether in the presence of air and light is thought to take the following course. A molecule of ether reacts in the presence of sunlight with a molecule of oxygen with production of hydrogen peroxide and vinyl ether—



Vinyl ether then undergoes hydrolytic fission in the presence of water giving alcohol and acetaldehyde—



The two substances acetaldehyde and hydrogen peroxide are now present and react as shown in the first equation. The views of Wieland and Winger seem to accord well with the mass of facts compiled on the autoxidation of ether by Baskerville and Hamor (*J. Ind. Eng. Chem.*, 1911, 3, p. 301) and with the recent experiments of Clowes on the autoxidation of ethyl ether (*J. Amer. Chem. Soc.*, 1923, 44, p. 1107).

Points of Practical Interest.—The occurrence of peroxides in anæsthetic ethers is rare because the latter are usually supplied by the manufacturers in sealed phials or tins containing a minimum amount of air. Peroxides appear in ether contained in badly stoppered containers, and factors favourable for the production of peroxides are, exposure to light and contact with air. Such ether, containing peroxides, is said to cause coughing, suffocation and even dangerous after-effects (Buxton's "Anæsthetics," 1907, p. 117) and when allowed to evaporate in an open vessel leaves behind a less volatile liquid residue which possesses a very pungent odour. Baskerville and Hamor recommend that ether for anæsthetic purposes "should be kept in completely filled, well stoppered dry glass bottles, preferably made of blue, green or brown glass, excluded from light in cool places and kept over mercury or preferably sodium."

Ether for anaesthesia, about which there is any doubt, should be tested for peroxides or acetaldehyde. The two best tests for peroxides are Jorissen's vanadic acid test and Baskerville and Hamor's cadmium potassium iodide reagent. Both are very sensitive and easily applied.

Vanadic Acid Test.—10 c.c. of ether shaken with 1 c.c. of vanadic acid solution should acquire no red colour. (The vanadic acid solution is most conveniently made from ammonium metavanadate, NH_4VO_3 and dilute sulphuric acid.)

Cadmium Potassium Iodide Test.—10 c.c. of ether shaken with 2 c.c. of aqueous 10 per cent. cadmium potassium iodide solution should show no yellow colour in the ether after one hour.

Ether containing peroxides can be purified by distillation over lime, caustic soda, or sodium.

Finally, I may say that from their experience of acetylene the Committee see no reason to recommend it as an anæsthetic. One of their chief objections to this drug is the impossibility of freeing it from acetone. Various efforts have been made in this direction but the conclusion come to is that the acetone can be effectually removed only by a system of washing through a tower fitted with blades or bearing rings of inert metal down which a thin stream of water is running. This is scarcely practicable in ordinary clinical work.

Discussion.—Professor J. S. HALDANE said that the paper brought anæsthesia into close association with coal-mining and its problems. Nitrogen as an impurity in nitrous oxide reminded him of the difficulty caused by that element in mine-rescue apparatus, which was a closed system of breathing, oxygen being supplied from a cylinder. If nitrogen was present, it gradually accumulated in the bag until it became suffocating, and there might be a fatal result, as the miner might be half a mile from the surface. Stringent regulations were therefore made about the oxygen being pure. Now it was obtained with less than $\frac{1}{2}$ per cent. of nitrogen. In the case of nitrous oxide he believed the nitrogen was dissolved in it. He used to think that if one took carbonic acid from a cylinder after one had blown out the top part, a gas free from oxygen would be obtained. But it was not so; there was always air dissolved in the liquid CO_2 , and it came out of the cylinder to the end. That led to a curious mistake. Professor Buckmaster thought CO_2 produced a spectrum like oxyhæmoglobin, but with pure CO_2 there was no such spectrum. Before the invention of the safety lamp, miners used a lamp which was turned round and caused a shower of sparks. They went into an explosive atmosphere, turning this for light. The spark, though its temperature was high, was unable to ignite methane; a hot surface was a very different thing from a spark. It was very necessary that the conditions required for an explosion should be realized. Thus the lowering of the percentage of oxygen would stop an explosion; it was very important to know whether an explosion would pass down a patient's throat. He was experimenting with Professor Lorrain Smith, of Edinburgh. There was a bag of pure hydrogen, and they wanted to see how long it took to feel the effects; Professor Lorrain Smith was to stop as soon as he felt anything abnormal. Suddenly that gentlemen went over backwards off the stool, and he (the speaker) caught him in his arms. He (Professor Haldane) then recognized that he himself had a lighted cigarette in his hand, but luckily it did not ignite the mixture down Professor Lorrain Smith's throat.

Dr. McKESSON said it was a lamentable fact that the fall in the price of nitrous oxide had to be used as a signal to keep a watch on the quality, as there might be a neglect of thorough washing of the gas, so as to add to the profits. In the United States such a period was now being passed through. His tests were the clinical reaction of the patient, and what his own nose told him. If the smell was not the right one, and especially if the odour was well marked, he did not use that supply. If the odour was slightly different from the normal, he might use it, but if the patient exhibited any abnormal symptom he at once turned off the tap. This was important, as he believed it was not yet known what were the reactions of gases under high pressures. It was also important to ascertain if re-breathing was used, and what was the solubility of nitrogen in the body compared with the solubility of nitrous oxide. Nitrogen was not a good anæsthetic, and it certainly interfered with the normal action of nitrous oxide when the latter was used as an anæsthetic.

In the United States there had been cases of fires in patients' respiratory passages, and in a very few instances there had been explosions and fire had followed into the depths of the lung. There was a case of ether and air explosion which occurred in Iowa. The cautery was being applied in a case of carcinoma of the tongue, the patient having received ether with the open mask. The mask was removed from the patient's face and the cautery applied to the tongue. An explosion immediately followed, causing fracture of the base of the tongue, and forcing the eyes out of their sockets so that they rested on the cheeks, with a hæmorrhage in the air-passages. Yet, unfortunately, the patient lingered some hours before succumbing.

Dr. WESLEY BOURNE said he had spoken on the subject at Glasgow, following on some work done in the Department of Pharmacology, when known quantities of impurity were added to pure anæsthetic ether. The effects of these mixtures were studied in the dog in respect of blood-pressure and recovery. Acid aldehyde, to the extent of less than 1 per cent., did no appreciable harm. The experiments were long ones, extending over three hours. Less than

$\frac{1}{2}$ per cent. of ether peroxide caused no noticeable harm, but up to 5 per cent. there was a definite effect on the blood-pressure. Sulphur compounds produced a foul odour. Ether mercaptan up to 1 per cent. did no harm at all. Ether sulphide produced a delayed poisoning which affected the alimentary canal; there was severe gastro-enteritis. Ketones were indifferent up to 5 per cent. and for three hours.

Dr. F. H. McMECHAN said there had recently occurred in the United States an interesting series of cases bearing on purity of nitrous oxide. He was sure the finer chemical tests would show the presence of nitric oxide. A chemist in the United States had discovered that nitrous oxide underwent decomposition in the fourth stage of compression in the cylinder on account of the temperature, which might be in the neighbourhood of 800° at that time. In order to eliminate any nitric oxide which might be formed at that point, the manufacturer had introduced Priestley's old method of reducing nitric oxide back to nitrous oxide by the presence of finely-divided metal. Recently the container for this was thought to be cumbersome, and so the body of finely-divided metal was cut down. Therefore the first batch of gas which went through, under the new conditions, gave identical results in the hands of four independent anaesthetists, namely, an absence of the cyanosis usually accompanying the drug until the thirty-fifth minute of the anaesthesia. Most of the observers were using the same type of apparatus. The gas was then examined and was found to contain minute traces of nitric oxide, though it probably would have passed all the Government standards. Oxygen did not relieve this lividity. He therefore hoped that the Committee, in its final report, would be very exigent about the elimination of nitric acid as an impurity. The standard of nitrous oxide purity in the United States was too low; 95 per cent. purity was not compatible with the best type of nitrous oxide anaesthesia; it should reach 98 or 99 per cent. The administration of nitrous oxide of a purity short of that became a difficult method of anaesthesia, especially for abdominal surgery. He would like to see standards of purity made extremely high, and to see manufacturers trying to live up to that ideal.

At a congress in Chicago the question was discussed as to what would happen to a patient who was submitted to ethylene-acetylene anaesthesia if when returned to bed he were allowed to smoke a cigarette, as patients often wished to do. Such a patient was allowed to light a cigarette twenty minutes after the operation and an accident occurred. A dog was given this anaesthetic; afterwards a match was lighted and thrown near its muzzle and an explosion in the air followed. It was thus an unsafe thing to allow such a patient to smoke a cigarette.

Professor J. S. HALDANE said that there were serious casualties in coal mines from nitrous fumes, and he had carried out animal experiments dealing with the subject. The cyanosis was that which was associated with nitrites, and it was due to the presence of methaemoglobin in the blood. It was not dangerous unless it became extreme. What he would lay stress upon was the danger of broncho-pneumonia of a fatal degree; the symptoms might not occur until twelve hours afterwards. This form of pneumonia was very deadly.

Dr. F. H. McMECHAN said that in the cases of casualty occurring in the United States the patients had not developed broncho-pneumonia, but in using the gas on guinea-pigs experimentally all had died in that condition.

Mr. G. WELLESLEY said he had taken a typical cylinder and worked down through every ounce. The first ounce contained an average of 8 per cent. of nitrogen, the second ounce 6 per cent., the third ounce 4 per cent., the fourth 4 per cent., the sixth 3 per cent., the seventh 2 per cent., and the remainder 2 per cent., though the thirtieth ounce gave only 1 per cent. nitrogen. There was an average of 2 per cent. throughout the cylinder. It would be easier to produce a purity of 98 per cent. than 95 per cent.

Dr. S. R. WILSON said that recently, in Liverpool, there occurred a death from acute fulminating pneumonia following eighteen hours after nitrous oxide administration; he did not know whether an analysis of the nitrous oxide used was made. He knew of two cases in which there was a fatal explosion in this country. One was at Birmingham, and in that case a bronchoscope was being used, and the vapour being inhaled exploded with a loud report. It did no harm beyond scorching the throat. In another case a flame reached the patient's mouth and the explosion ruptured the lung, death occurring from pulmonary haemorrhage. Twenty years ago, at the Manchester Dental Hospital, a complete chemical investigation was made of nitrous oxide, and reports of it were published in the dental journals of that time. The Committee's analysis closely agreed with the American analysis, except that in the American cases there was more definite evidence of impurity. When there were three or four

mishaps in succession, the fault was more likely to lie with the gas than with the administrator. The smell varied a good deal. It was a mistake to rely too much on the smell, as after a few hours of work the sensitiveness of the nose became somewhat blunted.

Dr. F. H. McMECHAN said that Professor Hallsley, of New Orleans, had done electro-cardiographic work in connexion with propylene. This drug was used as an anæsthetic in nine cases, in certain of which there was profound cardiac collapse after operation. He found in his laboratory that propylene, even in non-anæsthetic dosages, caused ectopic beats on the electro-cardiograph, and therefore Professor Hallsley had withdrawn his sanction of propylene as a clinical anæsthetic.

[July 15, 1926.]

Chairman : DR. A. F. H. McMECHAN.

Dr. F. H. McMECHAN (Chairman) said he would like to pay a tribute to the memory of one Englishman who to him had always stood for all that was best in anæsthesia, namely, Dr. John Snow. At one period in the history of anæsthetics (about the time that Snow began his work) anæsthesia for surgical operations was on the point of being abandoned, because methods for its continuous administration had not been properly developed. Accordingly Snow made a wonderful study of respiration and of the diseases which might be caused by impure atmospheres. He went into his laboratory and, as a result, delivered back anæsthesia to the practice of medicine. Had it not been for Snow and his work on the subject he (the speaker) very much doubted whether there would have been anæsthesia as it was now known. Snow was the first of a group of men in the British Isles, in Canada and in the United States who had had the temerity to make research, both laboratory and clinical, serve the purpose of practical application.

On an Attempt to Alleviate the Acidosis of Anæsthesia.

By WESLEY BOURNE, M.D. (Montreal).

ACIDOSIS in anæsthesia has attracted considerable attention during the past ten years. After much speculation and some controversy it has been definitely established, and in many instances frequently corroborated, that a true acidosis occurs in the anæsthesia of chloroform, of ethyl chloride, of ether, and to a less degree in that of nitrous oxide, of ethylene and of acetylene. The measure of a true acidosis is a lowering of the alkali reserve of the blood accompanied by an increase in its hydrogen-ion concentration. (The names of those who are responsible for this information are : Carter [1], Atkinson and Ets [2], Van Slyke, Austin and Cullen [3], Stehle, Bourne and Barbour [4], Leake, Leake and Koehler [5], and Leake and Hertzman [6]. Again it has been shown by Stehle, Bourne and Barbour [4], in the Department of Pharmacology of McGill University, that sodium and potassium are greatly increased in the urine after ether anæsthesia and more so when ether is preceded by morphine. Thus, it did appear that there occurs a neutralization of some acid or acids by these bases, and that the hypothesis of a compensatory migration of the alkali during anæsthesia from the blood to the tissues could no longer be tenable.

It next became desirable to know the acid or acids which passed out with the sodium and potassium, and further, if possible, to determine the source. Short [7] failed to find an increase of ketone bodies after anæsthesia, and Leake, Leake and Koehler [5] could find no tendency to the accumulation of ketone bodies or lactic acid in the blood of dogs anæsthetized with ether or chloroform.

Stehle and myself presented data [8] which "indicate that the excess of base excreted after a period of ether or chloroform anæsthesia is accompanied by an approximately equivalent quantity of phosphoric acid. The phosphoric acid appears to leave the muscles during the anæsthesia and to sojourn in the liver until the resumption of kidney function after the recovery of the animal, when it is redistributed and partially excreted."

The ability of the liver to store this phosphoric acid seems to depend on the degree of depression of the kidney function, and, accordingly, on the depth of narcosis.

"When morphine is administered as a preliminary to etherization a marked excretion of phosphorus occurs as soon as the ether is begun. This is attributed to an action of the morphine upon the liver which renders it incapable of retaining phosphorus. It is suggested that the low alkali reserve and increased acidity of the blood in ether anæsthesia is due to the discharge of phosphoric acid from the muscles."

Our efforts have not been entirely devoted to laboratory work, for we have already published the details of observations on a series of human subjects operated upon at the Western

Hospital, Montreal [9]. After ether, morphine and ether, chloroform and nitrous oxide there was a definitely increased phosphorus excretion in the urine. "The period of high phosphorus excretion does not always occur at the same relative time, but for the most part it is already evident in the course of anæsthesia. In the case of chloroform, the most pronounced increases occur in the post-anæsthetic periods, and this is true also in those cases in which ether was preceded by morphine." This difference would appear to be due to greater depression of kidney activity. Ronzoni, Koechig and Eaton [10] report marked increases in the lactic acid content of the blood during ether anæsthesia and correlate these with those of phosphoric acid; this harmonizes with the idea now held that the phosphates and carbohydrates are intimately associated in carbohydrate metabolism, there being a common precursor, as pointed out by Embden [11] in the form of a hexose phosphoric acid combination called "lactacidogen."

In accordance with these considerations of the acidosis of anæsthesia, and with the fact that the anesthetized individual loses sodium and potassium phosphates, it was thought advisable to administer these salts in somewhat the same proportions and quantities in which they were excreted. Two solutions were made up and labelled "A" and "B." One ("B") was distilled water with just enough magnesium sulphate to render the taste similar to that of the phosphate solution. This was used as a blind. The other ("A") was composed of 100 grm. KHCO_3 and 358 grm. $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$ in two litres of water; of this 65 to 80 c.c. were in some instances taken in a tumbler of water by mouth one hour before the time set for operation, and in other instances it was given in 1,500 c.c. to 1,700 c.c. of distilled water by the rectum, as soon as the patient was returned to bed, and as rapidly as was commensurate with its retention. In each case a questionnaire was filled in by some disinterested person—nurse or house-surgeon, who did not know the nature of the investigation—setting forth the following: (1) Pre-anæsthetic medication; (2) anæsthetic and method; (3) operation: (4) its length; (5) the time of return of consciousness, and (6) the extent of nausea. At once it is admitted that there are some factors which it is impossible to control, such as the peculiarities of the individual patient, the nature of the operation and its duration. I admit, too, that the results would be more convincing if the number of cases observed was greater. I have to thank Drs. Samuel Johnston and W. Easson Brown for their kind assistance in obtaining about one-half of these results at the Toronto General Hospital.

Nausea with solution "A"—phosphate mixture.

Extent	No. of cases	Per cent.
None	32	30.20
Slight	48	45.28
Moderate	13	12.26
Severe	13	12.26

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Nausea with solution "B"—a blind.

Extent	No. of cases	Per cent.
None	19	20.00
Slight	39	41.05
Moderate	20	21.05
Severe	17	17.90

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From these percentages it may be seen that there was less nausea in those patients who had had the phosphate solution. Again, calculating the average number of minutes of return to consciousness as against the duration of anæsthesia we find that with solution "A," 100 minutes of anæsthesia required 131 minutes for recovery, whereas, with solution "B," 100 minutes of anæsthesia required 141 minutes for recovery. Next, in terms of nausea, let us compare the results in those who had had morphine and atropine with those to whom none was given for both solutions, and they may be seen from the tables.

Nausea with solution "A"—phosphate mixture.

Morphine and atropine had been given.

Extent	No. of cases	Per cent.
None	11	27.5
Slight	22	55.0
Moderate	4	10.0
Severe	3	7.5

40

With solution "B"—blind.

Morphine and atropine had been given.

Extent	No. of cases	Per cent.
None	7	21.20
Slight	11	33.27
Moderate	7	21.20
Severe	8	24.33

33

With solution "A" and without morphine and atropine.

Extent	No. of cases	Per cent.
None	19	28.80
Slight	27	40.90
Moderate	10	15.15
Severe	10	15.15

66

With solution "B" and without morphine and atropine.

Extent	No. of cases	Per cent.
None	12	19.36
Slight	28	45.16
Moderate	13	20.96
Severe	19	30.52

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These facts are presented for what they are worth, and although they are rather meagre yet the following considerations are offered in their support:—(1) Nearly all of the cases reported upon received the phosphate mixture by mouth. (2) A certain definite but undetermined number of these were nauseated and vomited the solution either before anæsthesia or at induction; for this reason it seems a better plan to administer the solution by the rectum immediately after operation, and this is the method now adopted as a routine.

In conclusion, Nothmann, Wagner and Guttmann [12] of the Medical Clinic of the University of Breslau, have observed the changes in electrical excitability as well as the appearances of clinical signs (Chvostek's, Trousseau's, Mann-Erbsche's and Schulze's) in man when inorganic and organic potassium and sodium salts in acid, alkaline and neutral forms were administered by mouth and intravenously. They found that all of the potassium salts caused increased excitability. This potassium-ion effect was influenced by the nature of the anion, being greatest with that of the phosphate. The excitability was increased when the solutions were alkaline and diminished when acid. It should be desirable to increase excitability after the depression of an anæsthetic. Further, just recently Cloetta and Thomann [13], who have carried out some physico-chemical studies on the theory of narcosis at the Pharmacological Institute of the University of Zürich, present data to show that the calcium content of the blood is lowered from 8 to 15 per cent. quite regularly in the narcoses of ether, alcohol and somnifen (a barbituric acid derivative). This change runs parallel with the narcosis; as recovery takes place the calcium content returns to normal. With the administration of phosphates they found that sleep was shortened.

REFERENCES.

- [1] CARTER, W. S., *Arch. Int. Med.*, 1920, xxvi, p. 319. [2] ATKINSON, H. V., and ETS, H. N., *Journ. Biol. Chem.*, 1922, lii, p. 5. [3] VAN SLYKE, D. D., AUSTIN, I. H., and CULLEN, G. E., *Journ. Biol. Chem.*, 1922, liii, p. 277. [4] STEHLE, R. L., BOURNE, W., and BARBOUR, H. G., *Journ. Biol. Chem.*, 1922, liii, p. 341. [5] LEAKE, C. D., LEAKE, E. W., and KOEHLER, A. E., *Journ. Biol. Chem.*, 1923, lvi, p. 319. [6] LEAKE, C. D., and HERTZMAN, A. B., *Journ. Amer. Med. Assoc.*, 1924, lxxxii, pp. 1162-65. [7] SHORT, J. J., *Journ. Biol. Chem.*, 1920, xli, p. 503. [8] STEHLE, R. L., and BOURNE, W., *Journ. Biol. Chem.*, 1924, lx, p. 17. [9] BOURNE, WESLEY, and STEHLE, RAYMOND L., *Journ. Amer. Med. Assoc.*, 1924, lxxxiii, pp. 117-18. [10] RONZONI, E., KOECHIG, I., and EATON, E. P., *Journ. Biol. Chem.*, 1924, lxi, p. 465. [11] EMBDEN, G., *Klin. Woch.*, 1922, i, p. 401. [12] NOTHMANN, M., and WAGNER, A., NOTHMANN, M., and GUTTMANN, E., *Archiv. f. Exper. Path. u. Pharm.*, 1924, ci, pp. 17 and 28. [13] CLOETTA, M., and THOMANN, H., *Archiv. f. Exper. Path. u. Pharm.*, 1924, ciii, pp. 260, et seq.

Dr. McMECHAN (Chairman) said that before the meeting proceeded to discuss Dr. Bourne's paper there was a supplementary paper to be heard. In the discussion of his topic Dr. Bourne had laid stress on kidney function in relation to the acidosis of anæsthesia. The meeting was now to hear from Dr. Botsford, of the University of California, something in regard to the supplementary work which had been done clinically and experimentally on the kidney function in its relation more particularly to nitrous oxide anæsthesia.

Anæsthesia in Urological Surgery.

By MARY BOTSFORD, M.D. (University of California).

THE choice of anæsthetic in urological surgery has been the subject of much discussion and investigation in the past few years. That ether and chloroform inhibit kidney function is a well established fact, explained by Cushny as being due to the reduced blood-pressure and impaired aeration of blood.

The great progress that has been made in the development of local anæsthesia makes it the ideal method for the selected patient; but for the large proportion of cases where general anæsthesia is necessary nitrous oxide best meets the requirements of urological surgery. Unlike ether and chloroform it has no effect upon blood-pressure other than to cause a rise during secondary saturation when the oxygen percentage is reduced. As nitrous oxide is not eliminated by the kidneys, its obvious advantage has led to its becoming the anæsthetic of choice in most urological clinics where a general anæsthetic is indicated, and therefore the question of withholding the preliminary morphine, which influences so strongly the course of nitrous oxide anæsthesia, becomes a matter of great interest to the anæsthetist.

The work done by Haines and Milliken in the Surgical Research Laboratory and the Department of Urology, Graduate School of Medicine, University of Pennsylvania, on the subject of the renal effects of morphine and atropine with ether anæsthesia, suggested a

comparison with the results under nitrous oxide and oxygen. Seeking in their experiments to obtain a criterion of the operability of pathological cases, functional tests with intravenous indigo carmine were carried out, with and without morphine and atropine, both appearance-time and elimination being estimated, the latter being measured at three twenty-minute intervals. The results of these tests in six typical cases proved that elimination was slightly better after the injection of morphine and atropine, as shown by appearance-test and percentage of dye eliminated.

A series of six dogs were injected intravenously with indigo carmine after thirty minutes of deep ether anæsthesia, the etherization being then continued. The earliest appearance of the dye was not till twenty minutes had elapsed. The same dogs a week later were given morphine and atropine half an hour before etherization, and the appearance-time was four and five minutes, which was as soon as in the control cases and normal unanæsthetized dogs. They conclude from these experiments that morphine and atropine in the usual hypodermic dose does not effect the kidney function unfavourably and that in dogs it prevents the inhibition produced by ether. Because of the supposed retardation of the urinary secretion produced by morphine and atropine, it has been customary to omit it in cystoscopies and ureteral catheterizations under nitrous oxide, so this investigation was undertaken to determine whether nitrous oxide anæsthetization inhibited kidney function and, if so, whether morphine and atropine prevented this inhibition, as in the case of ether.

Cystoscopies in adults are usually carried out under some form of local anæsthesia, but here, again, the preliminary morphine would be of great value in counteracting the pre-operative psychic effect and promoting post-operative relief from pain, so long as it does not interfere with kidney function. Morphine is frequently the determining factor in the possibility of obtaining muscular relaxation under gas anæsthesia, and if, as Haines and Milliken suggest, it does not interfere with elimination, then urological operations which contraindicate ether and in which complete muscular relaxation is necessary—such as in the case of prostatectomies, both perineal and suprapubic, nephrectomies and operations on the bladder, as well as cystoscopies and ureteral catheterizations—may be done under nitrous oxide without the addition of ether.

The value of the pre-operative use of morphine in general surgery is still a matter of controversy. That anæsthesia is immeasurably benefited by its circulatory sedation, muscular relaxation, control of mucous production and the prevention of acapnia, due to psychic effect and slowing of respiration, is generally accepted.

One of the outworn traditions—that of its danger to children—is being gradually discarded. In the Children's Hospital, morphine and atropine, in properly graded dosage, is given almost as a routine before tonsillectomies, and in 40,000 cases, covering a period of thirty years, the records show no fatalities. Formerly, two years was the lowest age limit for the administration of nitrous oxide, even for induction, with the gas-ether sequence, but the increasing number of infants and young children in whom cystoscopies for diagnostic purposes were found necessary, led to the use of gas. Time is an important element in the safety of anæsthesia in infants, and the difficulty of ureteral catheterization, together with the occasional necessity for repetition at short intervals, positively contra-indicates the use of ether.

Hugh Young, in his recent work, deplors the fact that the diagnostic methods of modern urology are rarely called into use for the benefit of very young children, and he urges the publication of propaganda to prove to clinicians the desirability and simplicity of these methods. No doubt this attitude on the part of urologists is due to a realization of the dangers of ether and chloroform, and the impracticability of the administration of local anæsthesia in this class of patients by those with a lack of knowledge of the advantages and safety of nitrous oxide anæsthesia.

A review of seventy-six cystoscopies on female patients carried out at the Children's Hospital, San Francisco, showed the following results:

AGES FIVE MONTHS TO SEVENTY-TWO YEARS.

- Five cases under one year.
- Seven cases between one and four years.
- Ten cases between four and ten years.

Sixty-three patients were given nitrous oxide and oxygen, ten of these receiving varying amounts of ether in addition and five straight ether with gas induction; in five cases operation was done under local anæsthesia.

The records of voluntary micturition following anæsthesia show some interesting results.

(1) One patient, aged 5 months, who was cystoscoped four times with nitrous oxide and oxygen for periods of twenty-five minutes to one hour twenty minutes, voided urine one to two and a half hours later.

(2) Another, 5 months old (forty minutes under nitrous oxide), voided urine three hours later.

(3) A 6 months old patient (nitrous oxide and oxygen for one hour five minutes), who was given $7\frac{1}{8}$ gr. atropine, micturated four hours after anæsthesia; and a week later, after forty-five minutes of gas without atropine, in three and a half hours.

(4) A patient aged 32 (nitrous oxide and oxygen for thirty minutes), given morphine scopolamine $\frac{1}{2}$ gr. without atropine pre-operatively and again ten minutes after anæsthesia, micturated in two hours.

(5) One patient, 18 years old, given morphine scopolamine $\frac{1}{2}$ gr. and atropine $1\frac{1}{8}$ gr. preliminary to forty minutes of nitrous oxide, voided in one hour.

A résumé of the times of voluntary micturition shows a noticeable retardation in the cases in which ether was used, a slight one with atropine and none with morphine alone.

Observation of two cases in which the pheno-sulphone-phthalein functional test of 1 c.c. intramuscular injection was made, gave the following results:

Adult.—Cystoscopy and ureteral catheterization under nitrous oxide and oxygen, fifty minutes. Appearance test made at end of anæsthesia, ten minutes; and a week later with no anæsthetic, the appearance time was the same.

Girl, aged 8, cystoscopy and ureteral catheterization, nitrous oxide and oxygen, fifty minutes, appearance test made at end of anæsthesia $12\frac{1}{2}$ minutes, and without anæsthesia $12\frac{1}{4}$ minutes. No morphine or atropine was given in these cases.

The cases are too few to justify any conclusions being drawn, but the results would seem to show that nitrous oxide causes no appreciable inhibition of kidney function. The effect of morphine is somewhat contradictory, two of the cases show a retardation and one an acceleration of the appearance time.

In the Hooper Research Department of the University of California we duplicated the work of Haines and Milliken on a series of dogs, using nitrous oxide anæsthesia instead of ether. Because of the activity of the anti-vivisection movement at the time we were unable to obtain more than three dogs, and so our meagre results will later be supplemented by further work.

The dogs of approximately the same weight were injected intravenously with 1 c.c. of pheno-sulphone-phthalein without anæsthesia and the appearance time noted. Two days later the test was repeated under nitrous oxide anæsthesia, and after the same interval a third test was made under nitrous oxide anæsthesia preceded by morphine gr. $\frac{1}{4}$ and atropine gr. $\frac{1}{8}$ given ten minutes before anæsthetization, with the following results:—

	I	II	III	
	Male puppy	Male fox terrier	Female tan dog	
1 c.c. pheno-sulphone-phthalein intravenously	4 minutes	4 minutes	8½ minutes	appearance time
1 c.c. pheno-sulphone-phthalein intravenously	6 minutes	3 minutes	7 minutes	appearance time
N ₂ O - D	36 minutes	13 minutes	17 minutes	length of anæsthesia
Morphine gr. $\frac{1}{4}$; atropine gr. $\frac{1}{8}$; pheno-sulphone-phthalein intravenously	11 minutes	6 minutes	6 minutes	appearance time
N ₂ O - D	23 minutes	22 minutes	18 minutes	length of anæsthesia

Hypodermic of morphine and atropine given 10 minutes before anæsthetizing the animals.

Animals anæsthetized for 10 minutes or more before injecting the dye.

Discussion.—Dr. S. R. WILSON (Manchester) said he had got one of his own pupils to take blood reactions in acidosis cases, and in consequence of a complete clinical investigation the results entirely agreed with those of Dr. Bourne. It seemed to him that when one looked back on this age it would be classified as the physiological age in anæsthesia. They had at last reached a stage in which it must not be forgotten that the anæsthetist was not only concerned with the comfort and immediate safety of the patient but with his ultimate recovery.

He had been particularly interested in morphine, which he had given up using many years ago with nitrous oxide cases. He was inclined to believe, purely on clinical grounds, that his patients made better recoveries without it than with it. And that appeared to have reached a scientific explanation in the work done by Dr. Bourne. On the other hand, it might seem at first that Dr. Botsford's work was contradictory in that respect of Dr. Bourne's. But he did

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not think it was. Dr. Botsford's work applied to nitrous oxide eliminated by the lungs only, whereas the acidosis was especially seen with such anæsthetics as chloroform and, to a less extent, ether, where the excretion was by the kidney as well as by the pulmonary function.

Dr. T. P. KIRKPATRICK (Dublin) said that he had, some years ago, made investigations in connexion with the kidney function in anæsthesia, and noted the inhibition which followed ether anæsthesia. The impression he had then formed on the clinical grounds was that patients who were anæsthetized with ether for general surgical operations seemed to recover very much better and there was less trouble afterwards if they were not given morphia.

Dr. H. W. FEATHERSTONE (Birmingham) said he supported previous speakers on the lines that early, quick and uneventful recoveries from anæsthesia were more likely to be seen in the absence of morphia, particularly in cases in which there was some impairment of the renal function. It had been his practice to use nitrous oxide and oxygen for prostatectomy work, and he was quite certain that in very fragile patients (and he supposed one must always regard elderly men who had not had previous illnesses as being bad subjects for operation in that they were most susceptible both from the point of view of their livers, kidneys, and in other ways, to any drug) the result of the test seemed to be that nitrous oxide and oxygen was a highly innocuous form of anæsthesia.

Dr. SAMUEL JOHNSTON (Toronto) said that morphine, he thought, was a detriment to the average patient. In the first place, there was the probability of giving too much of whatever anæsthetic one might be using. Where morphine had been given the patient did not react in the same way. It was all very well for the expert, but with the teaching of students, of which one had to do a great deal, the student did not appreciate that the patient might be under sufficiently for the purpose of the operation, and kept giving more and more, loading the patient up with the ether. Naturally there would be a greater inhibition of the kidney function. Another disadvantage was the effect on the whole organism, which did not recover nearly so quickly. Morphine was given without it being ascertained whether a particular patient could take it or not; some patients were very much upset by it. Sometimes $\frac{1}{4}$ gr. proved too much. Many years ago he had discontinued the use of morphine preceding anæsthesia with the exception of the cases in which he was giving nitrous oxide and oxygen. He would prefer, even in prostatectomy, for instance, to use nitrous oxide and oxygen, and add just a little ether. It needed very little to get the necessary relaxation; ether given with, he was going to say, the gas machine—for it was about the most fool-proof machine he knew—a little quantity of ether merely to get relaxation, and then switched off. Dr. McKesson had overcome the use of ether by secondary saturation, but there was only one man he knew who could do that with safety. He had inadvertently accomplished it a few times, though he would not attempt it voluntarily. He would be afraid of his patient not coming to.

Dr. F. E. SHIPWAY said that for many years past he had been anæsthetist at St. Peter's Hospital, and of course the question of the anæsthetic had been of the utmost importance. His predecessors at St. Peter's had tried chloroform, ether, and mixtures of chloroform and ether, and had come to the conclusion that a mixture of chloroform and ether was the best for such patients. He, however, soon found that many of the patients were difficult subjects even under chloroform and ether for the particular operation which Sir John Thomson-Walker did. It was essential when the patient was in the high Trendelenburg position, when there was a tendency to difficulty of breathing, that the respiratory movements should be as slight as possible, and he had found the only way to get the absolute satisfaction the surgeon demanded was to abandon general anæsthesia and use spinal anæsthesia. He gathered from the large number of overseas visitors who visited St. Peter's Hospital that spinal anæsthesia was not much in favour; he believed the reason for that was that the dosage in the past had been too great. It was soon found that the average dose used for the old men was too great, but when it was cut down to half, the results were extraordinarily good. Now he used nothing but spinal anæsthesia with a very small dose of a general anæsthetic in order to keep the patient unconscious, and preceding administration he had no fear in those cases of giving morphine, or morphine and hyoscine. He had found that if one gave $\frac{1}{4}$ gr. morphine and $\frac{1}{100}$ gr. atropine to many of the alcoholic hospital patients the dose was not sufficient. With $\frac{1}{4}$ gr. morphine and $\frac{1}{100}$ th atropine the respiratory centre became so depressed that the condition was unsatisfactory. If, on the contrary, one gave morphine and hyoscine, the sedative effect was greater than with morphine alone and the respiratory centre was not so much depressed, because the action of hyoscine was partly that of atropine.

So that, contrary to the view of those who had already spoken, he took the attitude that with the older patients of the type he had at St. Peter's, morphine and hyoscine constituted the most excellent drug to give beforehand. The patients in his cases received as a routine $\frac{1}{16}$ morphine and $\frac{1}{16}$ hyoscine. In private practice where habits, breeding and education played a large part, such large doses could not be given. One-sixth gr. morphine was, as a rule, ample. He thought the fact that Sir John Thomson-Walker and himself, and he believed Dr. Hughes, had continued to give spinal anæsthesia over many years, showed that the results were satisfactory.

With regard to the effect of chloroform and ether on the kidneys it was difficult to say much, because patients were drained afterwards and the urine was not so easy to collect. But one of the anæsthetists at St. Peter's, being a Scotchman, and not converted to modern methods, still used chloroform for his cases and the Resident Medical Officers had told the speaker that there was a distinct tendency to uræmia on the part of those patients as compared with those who received spinal anæsthesia. The other anæsthetist in the hospital nearly always gave ether, so that there was a very good line drawn between the three. The patients of the latter did just, or very nearly, as well as those of Sir John Thomson-Walker. The only thing was that patients did tend to get more bronchitis in the winter than those who were submitted to a spinal anæsthesia.

Dr. Z. MENNELL said that all those who taught knew that in the cases in which the students did the work the patient very often took much longer to recover after the operation. Dr. Shipway had mentioned a point that had always been in his own mind with regard to morphine, and that was its effect on the respiratory centre. Surely the reason why those who had been given morphine took longer to come round—and they must all accept that as an undoubted fact—was because of the depressed respiration. They could not eliminate the anæsthetic in the manner in which they would if they had not been "doped." Personally, he hardly ever used morphine. It had gone out entirely as a routine in the two hospitals in which he worked, St. Thomas's and the National Hospital. He rarely gave nitrous oxide for genito-urinary work, because in his hands none of the machines, or other apparatus, would give him the relaxation which his surgeons demanded. There again, the perpetual question of the bottle cropped up. If they put ether, or chloroform and ether, in the bottle then, to his mind, they were begging the whole question. The anæsthesia was not gas and oxygen. It was gas-oxygen-ether-chloroform sequence.

He had seen Dr. McKesson do his secondary saturation at Toledo. All he could say was that he was a very brave man. He would not like to do it. Like Dr. Johnston, he had inadvertently done it and had been terrified.

He was interested in Dr. Shipway's point when he said that the patients at St. Peter's who had been given ether were attacked with bronchitis more commonly in the winter than in the summer. His experience was absolutely contrary to that. The cases which developed bronchitis were operated upon in the hot weather. At the present moment there was an unaccountable amount of bronchitis at St. Thomas's.

Nobody had spoken of atropine, and atropine only, without morphine. As he had said, he never used morphine but he invariably used atropine. He thought they could put on one side the statement which had been copied from text-book to text-book in England, that ether, with a small dose of atropine, without morphine, absolutely inhibited the secretion of urine from the kidneys.

Dr. J. D. GOLDMAN said he did not think a discussion on acidosis anæsthesia would be complete without some mention of the nitrous acids. As Dr. Wesley Bourne had said, acidosis was present in ether and chloroform and less so in nitrous oxide and oxygen. The work done, for instance, by Leake and Hertzman, Greene and others, had shown that with nitrous oxide and oxygen there was much less acidosis than with the vapour anæsthetics. The amount of work they had done on ethylene showed that with ethylene there was less acidosis than with nitrous oxide. Professor Leake had done very little, according to his last report, with acetylene, but he said that the little work he had done definitely showed that there was a marked difference between nitrous oxide and oxygen and acetylene, and that there was a difference between acetylene and ethylene; that the difference between acetylene and ethylene was similar to that between ethylene and nitrous oxide and oxygen. That was what would be expected. It was only those workers who had been careful to be as certain as possible of the percentage of oxygen that they used with the gas who knew how low a percentage of oxygen was used with nitrous

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oxide, for instance. With dogs, for example, 5 per cent. oxygen would give anæsthesia after nitrous oxygen, but if the percentage was increased by 1 per cent. there would be a marked slowing of awakening. If decreased by 1 per cent. the animal would be in a state bordering on great danger. There was thus in the case of the dogs a very small margin. His own experimental work had been with white mice, albino rats, rabbits and guinea-pigs, and much less with cats. In those cases there was no doubt in his mind, or in the minds of those who had seen the work done, that with nitrous oxide a very low percentage of oxygen was necessary; with ethylene a much higher percentage of oxygen was possible. It was true that when the first investigations were presented from ethylene it was generally stated that 20 per cent. oxygen could be used, and that statement, when checked later, showed that almost all the workers had used nitrous oxygen gauges, merely putting the ethylene in and allowing it to pass through nitrous oxide gauges, so that in those cases, when 20 per cent. was indicated it should be 12 or 13. In general, with ethylene it was possible to get round about 12, 13 or 14 per cent. oxygen; sometimes one had to go to much less, say, round about 8 per cent. In some cases one could go to much more, say, to 20 per cent. In those cases the condition of the blood would be similar, from an oxygen standpoint, to what it was normally, but in a great number of cases it was impossible to get the same amount of oxygenation as normally. It was only when one used acetylene that it was at all possible, in practically every case, to get normal oxygenation of the blood. Their own work had been chiefly from that standpoint, and it was possible to say definitely, comparing the three gases used, all rather fully, that with acetylene and oxygen a splendid colour was obtained throughout the anæsthesia. Work done in Germany had shown that the condition of the blood throughout three hours of anæsthesia was the same from an oxygen standpoint as that of normal blood, and it was those facts that explained why the research of Professor Leake definitely indicated that the amount of acidosis found with nitrous oxide and oxygen, which was much decreased with ethylene and oxygen, was still much further decreased with acetylene and oxygen.

Dr. WESLEY BOURNE (in reply) said he was glad Dr. Wilson had mentioned the work on alkalinity because it gave him an opportunity of saying that there was never any such thing in any anæsthesia of any kind. There was always a lowering of the alkaline reserve combined with an increase in the hydrogen-ion concentration. That meant acidosis. The lowering the alkaline reserve and an increase of hydrogen-ion concentration was nothing more than a lessening of the ordinary alkalinity of the blood. As they knew, the blood never became acid in life.

In the first place, as to morphine, he agreed with many concerning the advisability of using it. One reason against the use of morphine was that it enhanced the acidosis. It increased the outpouring of phosphoric acid from the muscles, which was very marked. An important argument in favour of the use of morphine was that it always offset the ordinary blood-concentration which ether and chloroform invariably caused. The blood-concentration with chloroform and ether was something like this: Supposing before an anæsthetic the total blood-solids were 18 per cent. With ether they would go up as high as 24 or 25 per cent. That was a tremendous increase in blood-solids and indicated an excessive lowering of the fluidity of the blood. Morphine offset all that. That was a very strong argument in favour of using morphine. Another very strong argument in its favour was that it always offset the oliguria or anuria which ether and chloroform caused. On the other hand, as against the use of morphine it should be remembered that it produced nausea, which was in some instances very marked; it interfered with the peristalsis of the bowels and depressed the respiratory centre, though this depression could be very well countered by the use of carbon-dioxide. With regard to anuria anæsthesia, it was a curious thing that that anuria was one of water only; the solid compounds of the urine were not interfered with; they came out in the same proportions as if ether or chloroform had been given.

Dr. MARY BOTSFORD (in reply) said that it appeared from the discussion that the anæsthetists who used gas-and-oxygen were almost all in accord with her own view of the matter, that morphine was of great value. With ether the feeling was somewhat different. In replying to some of the remarks made, it seemed to her that those anæsthetists who had been doing much work in connexion with urological surgery mostly felt that gas-and-oxygen was preferable even to chloroform wherever it was possible to use it.

She had taught for thirty years, and having used morphine for thirty years she had yet to find cases in which there had been bad results. It was her custom to

set the student to give, say, an anæsthesia for prostatectomy, sitting by and supervising to such an extent that she herself really gave the anæsthetic. Naturally a student was apt to give a little more anæsthetic than an expert, but the idea of a student giving more anæsthetic because of the morphine was exactly opposed to her own feeling. In fact, she (Dr. Botsford) felt that the greatest value of morphine was that a patient who had had a preliminary narcotic did not require so much ether or chloroform. In other words, that the morphine produced relaxation of the muscles, which saved the patient that much of the anæsthetic material, and that was the chief reason for giving it. As to recovery not being so rapid and the general organism not reacting so quickly after morphine was given, she felt that that was a question affecting the ether rather than the morphine. As regarded the idiosyncrasy, that, of course, was very easily discovered. There were many patients who would say that they had an idiosyncrasy, but it was purely imaginary. They would say that morphine made them nervous and irritable. If it was given therapeutically it did not make much difference; one obtained a relaxed effect on the muscle tissue and so forth, and in this way it was easy to discover the real idiosyncrasy.

In a recent work by Hugh Young, the "Manual of Urology," which had just appeared, there was an interesting series of results in prostatectomies, 400 cases being reported. The method at the Johns Hopkins Institute was to give ether, largely. Of 400 cases only 150 were straightforward gas-and-oxygen anæsthesias. Dr. Young reported 4 per cent. deaths. In investigating the pathological reports in Dr. Young's book, the speaker found that many of the deaths were due to pneumonia, and of 400 anæsthesias 150 were gas-and-oxygen. Probably the success of that work was due to ether.

Spinal anæsthesia was superseding the various anæsthetics to a large extent in every possible case, but there was a saying to the effect that any clinician who was using local anæsthesia to any large extent was well on the way to gas-and-oxygen anæsthesia.

Dr. F. H. McMECHAN (Chairman) said there was one point made by Dr. Bourne which he would like to stress, and that was with regard to the fact that potassium had the peculiar effect of causing excitability. At one of the Congresses in the United States delegates had had the pleasure of having Professor Hughes of the Agricultural College of Kansas with them to discuss the therapy of anæsthesia, and Professor Hughes had brought out one point which referred to Dr. Bourne's work. If it was wished to make a record of the balance in the human body as between excitability and sedation, sodium and potassium were put above the line; calcium and magnesium below it, and the proportions of sodium and potassium, calcium and magnesium were written behind those words. Then if it was found that a patient needed to be stimulated and excited, that patient was put into the sodium or potassium testing. If, as Dr. Wilson had said, it was possible to begin the study of anæsthetics in this physiological era more from a basis of pure science, it might be possible to raise therapeutics to a much higher level. The fact of the matter was that Dr. Bourne himself was quite in agreement with the Emeritus Professor of Medicine of the Post-Graduate College of New York City in that he had found that dio-sodium phosphate was the alkalizing agent which was most useful in combating a dys-function of the kidneys and in reversing the acidosis of anæsthesia. He (the speaker) hoped others would consider certain vital processes along the same lines, particularly in reference to anæsthesia, and that the results would be carried over into clinical work.

Gas-and-Oxygen Anæsthesia In Abdominal Surgery ; and "Secondary Saturation."

By E. I. McKESSON, M.D. (Toledo, U.S.A.).

Dr. E. I. McKESSON said he would deal with the subject under three heads: First, preparation of the patient, which had already been fairly well discussed; secondly, the difference in signs and symptoms of pure gas-oxygen from other anæsthetics; thirdly, the shortcomings of apparatus which reflected on the difficulty of securing anæsthesia of a satisfactory grade in the patient.

In regard to preparation of the patient, pre-medication in some form or other was usually necessary. One must be careful in making dogmatic statements that one always used morphine, always used atropine, or always used hyoscine. That was not so. The condition of the patient had a great deal to do with what preparation or what pre-medication was employed; whether the patient had lost blood in any sense; whether the patient was toxic to a degree;

whether there was acidosis, so called, which might be undiagnosed or misdiagnosed by the surgeon, by the anæsthetist, or anybody else who had charge of the patient. So that in making a statement regarding pre-medication he would say he *usually* employed $\frac{1}{4}$ gr. of morphine combined with $\frac{1}{160}$ gr.—no more—of scopolamine or hyoscine. The desirable way in which to administer morphine usually was to divide the dose, a $\frac{1}{8}$ of a grain first and then $\frac{1}{8}$ of a grain from one and a half to two hours before the operation. One often missed the time because of various conditions, such as slowness in the pre-medication. Sometimes the estimation of the hypodermic or the hypnotic was wrong entirely, so that the good effects desired from pre-medication were lost, and then it became necessary to supplement pre-medication by further medication on the table with not quite so satisfactory results. However, since morphine or some hypnotic was usually necessary in beginning the abdominal operation under nitrous oxide and oxygen, he considered that a small dose of morphine was not out of order. One obtained the result of the second dose of morphine on the table within fifteen minutes.

As to atropine, he had never used large doses such as he had heard had been used by Dr. Shipway, and had no experience of its action under those conditions. The dose usually employed was $\frac{1}{160}$ gr. when it was used, and he had found few occasions when it was necessary to employ atropine purely from the physiological standpoint or the pharmacological point of view, when he was using pure nitrous oxide and oxygen in the case. He granted at once that atropine might be very desirable when using ether, but he could not subscribe to the use of atropine as a routine in nitrous oxide and oxygen cases. Preferably he and his colleagues used scopolamine. If the patient was old or exceedingly young, then no scopolamine was used, reliance being placed on morphine only, without atropine.

With regard to the second aspect of the subject—the difference in signs between those arising in pure nitrous oxide and oxygen anæsthesia and those of nitrous oxide-oxygen with a very little of each—he would say candidly that for two years in the work in one hospital he had had no other attachment on the machine, nor had he used ether in a single case, so that a pure gas-oxygen as against gas-oxygen with ether made all the difference in the world as to the symptomatology of the patient. Ether added to gas-oxygen produced the true signs of oxide-oxygen, and when added, to a very marked extent and with an enclosed inhaler such as was used in gas-oxide, a small amount of ether became a relatively large dose. So that the ether used really dominated the picture from a clinical and from a scientific standpoint.

If one gave gas-oxygen pure without ether, one obtained these differences in signs. When a patient swallowed, retched and vomited or merely swallowed, as the first of the series of movements with gas-oxygen, one could be quite sure in 8 per cent. of the cases that the patient was in too deep anæsthesia. If ether was in the machine and dominating the picture, one knew the patient was not deeply enough under. He passed through that stage years ago. He had not realized that fact, and in trying to put the patient more deeply under he always precipitated vomiting. He found that giving a strong percentage of oxygen to stop the nausea corrected that symptom rather than augmented it.

Respiration was altered from the normal under nitrous-oxide anæsthesia. It was usually increased in speed; sometimes in depth; sometimes in both. Usually an increase in the ventilation resulted from the administration of nitrous oxide and oxygen, without morphine. With morphine in proper doses and properly timed, with anæsthesia maintained at a smooth level, then the augmentation of ventilation was offset, so that instead of having a ventilation of 20 litres per minute,—the patient breathing rapidly and panting, there was one of 8, 7, 6 or 10 litres per minute, more near the normal. That was one advantage of morphine and one of the reasons why it was used. Why? If a patient breathed forty times a minute, the very act of such rapid respiration was laborious and led to muscular exhaustion of the patient, and muscular exhaustion had a very marked influence on the outcome of the operation immediately, and eventually on the patient. Muscular exhaustion through rapid respiration was to be discouraged and avoided as far as possible, and the administration of morphine was one of the ways of bringing that down to the normal.

If the anæsthetist "re-breathed" the patient he did it for two or three reasons. One, in order to prevent over-ventilation, while allowing the patient to ventilate. It was more scientific and clinically more desirable to prevent over-ventilation by the proper use of morphine and the careful administration of the anæsthetic than to treat the symptom. Thus "re-breathing" was used when it was necessary to balance the ventilation and keep it down to normal in spite of allowing the patient to over-ventilate. Another purpose of "re-breathing," if morphine had acted a little too strongly, was to deepen the respiration, and thus to increase the expansion of the lungs.

Another difference in the signs of anæsthesia between nitrous oxide and oxygen and other anæsthetics was a matter of cyanosis. Cyanosis was not a sign of anæsthesia, and never had been. It was certainly not a guide to gas oxygen. Muscular signs were the only signs which could be relied upon as guiding signs regarding the depth of narcosis, because it was a fact that if a patient had a small amount of hæmoglobin in the body, and low percentage and small volume, it was impossible to cyanose such a patient; it was possible, and, in fact, very easy, to over-ventilate that patient. On the other hand, the full-blooded patient, with a large volume of hæmoglobin, might be slightly cyanotic while breathing ordinary air, so that the colour was not a guide to anæsthesia. The colour might be used to indicate when one was reaching the limit of anæsthesia, but it was seldom dependable when it was a question of maintaining the exactly right or proper level of anæsthesia; cyanosis in that case was a very poor means of indication. The respiration, the pupillary signs and other muscular phenomena were better guides. The first, of course, was respiration. The desirable thing in respiration was to secure smooth, quiet breathing as nearly normal as possible; if too shallow, then to increase it slightly by "re-breathing."

Secondary saturation with reference to abdominal surgery seemed to be largely misunderstood. Since his first paper, in fact his only paper on the subject, was written he had seen every possible interpretation of what was said. Secondary saturation was nothing more nor less than carrying the patient into a deep anæsthesia. Everyone who succeeded in the administration of nitrous oxide and oxygen did that, whether he called it by the name he used or not; and he did it in one of two ways: by the slow method, which was the usual method, or by the rapid method, whereby he caused himself and his observers some concern because of the rapid changes that took place in the appearance of the patient. Unfortunately his (the speaker's) first description of secondary saturation was of the rapid method and it had done nothing but scare people ever since his paper had been written. He had hesitated for several years to write because he feared that that result would be the outcome. He would now describe the method once more.

First, the rapid method consisted in having induced anæsthesia by primary inspiration. At any time after that, if a larger or a deeper anæsthesia was desired or a larger amount of nitrous oxide was necessary in the blood-stream one could proceed as follows: either set the machine for less oxygen than the patient would tolerate temporarily, or set the machine for no oxygen whatever, allowing the patient to breathe the high nitrous oxide mixture until symptoms of profound anæsthesia, or approaching the fourth stage, but not the fourth stage, appeared.

What were the symptoms? (1) Dilated pupil. That happened with ether. (2) A pupil which did not react to light. (3) Prolonged inspiration. (4) Rigidity of the general muscles. (5) Rigidity of the skeletal muscles. If the secondary saturation was done in the early stages of narcosis it was accompanied by jactitation. If it was done in the later period of anæsthesia it was not accompanied by jactitation, but merely by rigidity. In other words, it was an attempt to put a little more nitrous oxygen in the blood-stream and tissues than was there before. Before the patient stopped breathing he gave the oxygen and induced the second stage of secondary saturation, thus overcoming the rigidity which had been produced by the first procedure. The patient was more relaxed than he had previously been. If one gave too much oxygen the anæsthesia was disturbed and the patient was returned to the state of reflex rigidity which perhaps had existed before.

The slow method consisted in merely cutting down the oxygen percentage that was administered by one, or perhaps two per cent., and continuing the narcosis until the accumulation of nitrous oxide produced signs of anoxæmia. Then one breath of 25 to 30 or 50 per cent. oxygen to further develop anæsthesia. That was the usual and the best method. If he was in a hurry and wanted to produce anæsthesia of a fairly deep degree with maximum relaxation then he resorted to the rapid method, cutting off the oxygen entirely and carrying the patient up to approaching the fourth stage, but not stopping respiration.

Occasionally they might take respiration as having stopped, but one did not care to wait to see if that was so. In that case one wanted to put oxygen into the lungs, and so provision was made for inflating the lungs with oxygen. And that brought up the question of apparatus. One should not attempt to give nitrous oxide and oxygen in abdominal surgery unless one was prepared to inflate the lungs with oxygen in case of working a little too close to the margin of the fourth stage. Ability to force oxygen into the lungs was one of the things which made it possible to "dope" the patient with nitrous oxide a little deeper than was done by most anæsthetists. It was the assurance that one could bring the patient out, without any

difficulty, without the surgeon knowing that anything had happened, without the surgeon knowing, perhaps, that the patient had hesitated in respiration.

The greatest difficulty in giving oxygen in that manner was that one might give too much and the patient become too far out and thus disturb the level of anæsthesia. It might seem unnecessary to say that the first requisite to a deep nitrous oxide and oxygen anæsthesia was a definite dependable mixture of two gases, a mixture which was maintained, not produced, not necessarily a mixture of which one knew the composition. It did not matter so much just whether one knew exactly what proportion of nitrous oxygen there was in the mixture, but it was necessary to know if the preparation varied after one had set it. That was one of the most important factors in maintaining a deep narcosis on nitrous oxide.

The second point which helped a great deal in abdominal surgery was the use of pressure. The gas was under pressure. If the gas was not administered under pressure there were times when there was more or less interference with respiration. The patient was unable to breathe freely. The lungs were not properly filled; the absorption of gases was imperfect and therefore the anæsthesia was lighter for a time than it would have been had the patient breathed deeply, or as usual. Under those conditions a little pressure was used to assist the expansion of the lungs, to make it easier for the patient to fill the lungs; in fact, as it were, to push the gases in.

There was something else that happened at the same time if there had been faulty adaptation of the inhaler. If there were leaking points between the source of gas and the patient which allowed air to be drawn in, even in small amounts, the anæsthesia was affected. Working under pressure encouraged the waste of gas and inspiration of air through those leaks, and so one would be tempted to attribute to the use of pressure, conditions which were not really due to the pressure itself but to the elimination and the leakage of air.

At any rate, the pressure itself did increase the absorption of gas. Even though it was very small, though one might be working only under two or three millimetres of positive pressure, there was a slight difference due to the pressure *per se*.

Dr. C. W. MOOTS (Toledo, U.S.A.) said that thirty-one years ago he commenced surgery with the idea of enabling the patient to return to work in the briefest possible space of time with the least inconvenience to himself and in the best possible conditions. Those were the days which the Chairman had mentioned when one used as an anæsthetic only chloroform or ether or a combination of both, and sometimes a little alcohol. During that time (say in 1906) he came into touch with Dr. McKesson, and in conversation with one another they found that they had something in common in connexion with surgery. They made up their minds that they would get together as surgeon and anæsthetist. He believed that was the really important point in the whole matter. It mattered not so much, probably, what agent was used, as that both the anæsthetist and the surgeon should be men with ideals. In the days of which he was speaking there were no professional anæsthetists. He was glad to think that the encouraging work done by the Association was going to change the whole attitude towards surgery in a few years' time. He must compliment Dr. Johnston on the fact that there had recently been taken into the hospital with which he (the speaker) was connected, two graduates from Dr. Johnston's institution who did secondary saturation just as well as did Dr. McKesson.

Dr. McKesson had referred to the preparation of the patient. It would be well if he said that Dr. McKesson gave anæsthesia for a number of surgeons, each of whom probably had a few peculiarities! His (Dr. Moots') own was that he wanted to begin with the patient the moment he arrived at the front door of the hospital, and he would not work in a hospital which did not try to do what he wanted. He wanted the patient to be received pleasantly and to feel at home in the hospital. He did all he could to get rid of every adverse effect, from the time the patient entered the hospital to the time he left. That was done with the aid of intelligent nurses, superintendents and others. He was in favour of the use of some little sedative, something like sodium bromide, the moment the patient was brought into the room. In fact, the patient was kept fairly sleepy all the first day and night. In the morning, two hours before the operation, the patient—if an ordinarily-sized woman—received $\frac{1}{2}$ gr. morphine and $\frac{1}{200}$ gr. scopolamine, which must not be in tablets, for they were badly made up in his country. One hour before the operation the patient was given a similar dose, and by the time of the operation, if Dr. McKesson was late, the patient did not care much what happened. She was as happy as they had all been on the previous evening. She was not scared. He had not heard anyone mention the argument that although morphine lowered the metabolism in general, it nevertheless, rested a person very much. He used it, and, as far

as he could see clinically, after twenty years' experience, there had been no bad result from it. Of course every case was not treated in that way; it was wrong to have a routine procedure for every human being.

It was arranged, as far as possible, to have everything quiet in the operating room. There were no unnecessary assistants; just sufficient to work the apparatus, which was very simple. Whilst the work was not done hurriedly, it was done in the shortest possible time. If it was found that one method was a little slow, they worked at something else until there was more rapidity.

The great difficulty came when the surgeon made the incision; when nitrous oxide and oxygen were used, the average surgeon felt he could not operate. It was up to the surgeon to learn that it was possible to operate without having a practically dead patient. For instance, with his appendix operations he preferred the patient to be somewhat rigid. The incision was made and, if the patient was somewhat rigid and breathing fairly well, then immediately the peritoneal incision was made the appendix came out. The practice was to give as little anæsthetic as possible and to operate as soon as possible. The patients were not kept in bed a long time after the anæsthesia. He liked them to be up the next day and sitting in a chair. Throughout the war he had all the men who had undergone appendicectomies up the next day. In that way he avoided the dread of a long time spent in hospital and, more important still, he avoided adhesions becoming serious by getting the patient in the upright position. Probably some adhesions would form, but if the patient was in the upright posture they did not drag or pull as they would if the patient was kept on his back for weeks following operation.

He might add that he, personally, used a gas machine without any ether attachment at all, and had done so since two years before the war. Occasionally, a little ether was used, because it was believed to exercise less chemical effect than other anæsthetics. The difficulties in regard to chloroform and ether were all chemical, but it was a hard question to deal with and solve. The administration of nitrous oxide and oxygen, and probably atropine, were very largely technical. It ought to be possible to overcome the technological difficulty.

Mr. H. E. BOYLE said that he also had seen Dr. McKesson do a case of secondary saturation and, candidly, it had frightened him. Nevertheless, he was glad to have seen it, because he himself had inadvertently done a secondary saturation and immediately knew what to do to prevent ill effects arising. Although he gave a great deal of gas and oxygen, he found he obtained more even anæsthesia if he gave a little ether as well, and in cases of prostatectomy he could also better get that degree of relaxation which English surgeons demanded. At the present day, for abdominal work he practically always used intratracheal gas-oxygen-ether, and once having got the patient going and steady for about ten minutes, it was only necessary to use very little ether. He was interested in hearing what Dr. Moots had said with regard to rigidity, but there was hardly a surgeon in London who would operate on a rigid abdomen.

Dr. Z. MENNELL said he had great admiration for the work he had seen Dr. McKesson do, but he contended that it was impossible, under gas and oxygen, to get the slack abdomen that English surgeons demanded. And when he heard Dr. Moots say he preferred to see the appendix slip out of the wound, all he could say was that Dr. Moots' attitude towards surgery was entirely different to anything known in England. If he had given an anæsthetic for any of the surgeons he worked with and that occurrence took place, he (Dr. Mennell) would never expect to give another anæsthetic for them. He was speaking, of course, of gas and oxygen *per se*. Dr. McKesson begged the question when he spoke of scopolamine and morphine, especially when he referred to a second dose of morphine on the table. Dr. McKesson had made one great admission when he said he gave morphine to depress the respiratory centre, which was rather giving himself away. Surely when administering an anæsthetic one did not want to depress the respiratory centre. Unfortunately, during his visit to Toledo he had only seen Dr. McKesson do his secondary saturation by the quick method, and he (Dr. Mennell) would say that the symptoms of profound anæsthesia which resulted were identical with those of impending death! He had seen the patient cyanosed, not breathing, with pallor coming on. He realized, however, that he was with an expert and that nothing untoward could happen; and it was so. But he thought Dr. McKesson very nearly burst the patient's chest open with oxygen before the patient came round. The gas was used under enormous pressure. He maintained that every anæsthetist before taking up his specialty should have sewn up an abdomen; he would then realize the difficulties more than he was apt to do as a pure

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anæsthetist. There was no trouble in sewing up a lax abdomen. Dr. McKesson had referred to jactitation and to the patient swallowing when deeply under gas and oxygen. To his mind, both those things implied rigidity. He had never before heard that swallowing, with gas and oxygen, was a sign of deep anæsthesia. He had always regarded it as a sign of light anæsthesia. Then Dr. Moots had referred to adhesions and the value of gas and oxygen in preventing them. To this he could not agree. Surely adhesions were formed for the most part by trauma, and if one had a rigid abdomen no surgeon, however expert, could do his work without traction of the peritoneum, and that must form adhesions. With regard to Dr. Boyle's reference to intratracheal gas and oxygen, there was one point with which he could never agree. It was necessary to have a fairly deep anæsthesia and relaxation before one could pass the catheter. He (the speaker) would be very sorry to have a catheter passed down his own throat under gas and oxygen.

Dr. C. LANGTON HEWER (London) asked what was the condition of the heart before Dr. McKesson used oxygen, and whether in the case of cardiac degeneration there was any danger of rapid dilatation of the heart and death. As to Dr. Mennell's last point, although it was necessary to get the patient deeply under at the beginning, when the catheter was once in position one could run on very little ether indeed.

Dr. F. E. SHIPWAY said he wondered whether the amount of morphine given in Dr. McKesson's cases was not largely responsible for the satisfactory results which he claimed. If one gave large quantities of morphine it was possible to depress all the functions so much that one could almost operate on a patient without anything at all. As he had said in a paper read years ago, it was necessary to be quite clear what they were talking about. It was not unusual for the words "gas and oxygen" to be used when what was actually meant was gas, oxygen and ether. Therefore statements made were somewhat misleading and created a wrong impression. He had never seen anyone produce relaxation in the average upper abdomen with gas and oxygen alone.

Dr. S. R. WILSON agreed that there must be no bottle whatever on the gas and oxygen machine. The number of cases of diabetes coming up for operation had increased so enormously since the war that he believed that even a little chloroform or ether in those cases did incalculable harm. He considered he had failed if he could not carry his cases through on gas and oxygen alone. Fortunately, with an extra degree of toleration on the part of the surgeon, it had been possible to carry some cases through, but those were the patients who were very ill. If a patient was relatively fit and well and strong, with full muscular development and a full percentage of hæmoglobin, then, in his experience at any rate, it was impossible to get the relaxation required by English surgeons without the addition of some ether. As regards preliminary medication, he agreed that morphine was important, though he hesitated to give as much as Dr. McKesson did. He would not like to try to do an abdominal operation under gas and oxygen without some morphine. With regard to Dr. Moots' remarks with regard to a rigid abdomen and the appendix slipping, as a rule if an appendix and gall-bladder protruded they ought not to be removed!

Dr. T. P. KIRKPATRICK asked whether in the case of intratracheal gas and oxygen the catheter was a large one, or one only occupying about half of the capacity of the trachea. In the cases to which Dr. McKesson referred, of positive pressure during the continuance of the gas and oxygen after the secondary saturation, was an increased hæmorrhage from the site of operation observed owing to the damming back of blood by the intratracheal pressure?

Mr. H. E. BOYLE explained that he employed quite a small catheter, and did not use a great deal of pressure with the gas.

Dr. MARY BOTSFORD gave details of experience gained in intratracheal gas and oxygen during the war at the Military Hospital at San Francisco, when she worked with the chief surgeon, Major Robertson. Major Robertson, who was very much interested in intrathoracic surgery, evolved the method of using an ordinary genito-urinary stilette, moulding it to the shape of the pharynx and then introducing it into the catheter. That was found to be a very simple method, and it was possible to carry it out without the least degree of traumatization. It was possible to do very much better work with gas and oxygen, and there was no necessity for catheterization. With positive gas and oxygen it was absolutely unnecessary to catheterize.

Dr. T. P. KIRKPATRICK said that he had no experience of the use of nitrous oxide and oxygen in abdominal operations, but had always found, with the ordinary administration of nitrous oxide and oxygen, that it was easier to obtain satisfactory results when the barometric pressure was high. It was possible that those not very expert at the method might obtain good results on days when there was a barometric pressure of 31 in., whilst the difficulty would be very much greater on a day when the barometric pressure was down to 29 in. He agreed that one of the most important things in connexion with any anæsthetic was collaboration between the surgeon and the anæsthetist. Surgeons sometimes required the patient to be anæsthetized until he became absolutely flaccid, when, with a little consideration and care, and perhaps a little extra trouble to the surgeon, it would be possible to work with a less degree of relaxation and with quite satisfactory results to the patient.

Dr. MCKESSON (in reply) said that it was quite possible to work for a surgeon for twenty years and still hear him express dissatisfaction. He had heard a surgeon actually say, while putting traction on the lower margin of the rib, that the patient was not relaxed, and the assistant called the surgeon's attention to the fact that the instrument was pulling on the ribs and that he had already fractured one! The patient was not rigid! The surgeon was not satisfied! Had they ever heard a surgeon express the hope that the anæsthetist would die? Could they believe that a surgeon could go to such extremities to discredit a method or a person? He would. But co-operation between surgeon and anæsthetist was essential to success in anaesthesia by any method, and he was very glad to say that for some time back he had had that co-operation and still had it. Dr. Moots was the first to afford him that co-operation, and partly on that account Dr. Moots had been very successful, not from the standpoint of the anæsthetist but from that of the patient. Just because one used morphine to get good results with nitrous oxide, it did not necessarily mean that it must be used. He had heard, whilst in this country, of some things he might use when he returned to America in order to avoid some of the post-operative nausea due to morphine. As to Dr. Mennell's remark with regard to the depression of the respiratory centre, he (the speaker) pointed out that the lowering to a normal state was the purpose of the use of morphine with nitrous oxide. The patient's respiratory centre was stimulated, and when one gave morphine one brought it down to normal. That was the correct method. He had had very little experience in connexion with intratracheal administration of nitrous oxide; in fact, he had never thought of passing a catheter into the trachea. In an ordinary gas-and-oxygen anæsthetic he made pressure take the place of the catheter. Possibly it would be better to try the catheter. But it might be necessary to put the patient under ether in order to introduce the catheter. Regarding swallowing as a sign of right anaesthesia, that was true with ether but not so with nitrous oxide. He was glad that Dr. Hewer referred to the condition of the heart in secondary saturation. At the time they were beginning to use nitrous oxide and oxygen (about 1906), he began to observe blood-pressure and respiration and charted the results. He thought that whatever success he had experienced in anaesthesia had been very largely due to the study of the patient during operation by means of blood-pressure, pulse and respiration observations. That did more than merely keep the anæsthetist busy and alert and acquainted with the real condition of the patient. It interested the surgeon, it secured that co-operation which the anæsthetist so much needed. If the anæsthetist showed the surgeon that he was interested in the patient to the extent of giving oneself a great deal of additional trouble, and if one showed the surgeon the chart with the details noted, he immediately secured the surgeon's interest and attention, and from that time onward the surgeon would co-operate with the anæsthetist to the fullest reasonable extent. Such education, if he might say so, of the surgeon had been largely responsible for whatever success he (the speaker) had had.

As to the amount of pressure, he rarely exceeded 3 or 4 mm., and with that amount in a nitrous oxide machine the pressure was really quite a small one. When one spoke of pressure in the lungs it was not meant that the pressure was continuous; it was intermittent. He was glad to hear Dr. Kirkpatrick raise the question of barometric pressure. He had personally observed that on certain days there were a large number of cases in which the patients had nausea, whilst on other days there was no nausea. He used to think that the nausea was brought about by a slight difference in the gas used. But he then began to watch the barometric pressure, and, surely enough, if the day was clear and the barometric pressure high very little nausea occurred; on the other hand, with a muggy day and a low barometer there was a great deal of nausea. He thought that a low and rapidly falling barometer had the same effect as an aeroplane trip in causing marked sickness, and that low barometric

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pressure, coupled with the low oxygen which was employed in gas-oxygen anæsthesia, produced nausea more promptly than would be the case when the barometer was high.

Dr. Z. MENNELL asked if Dr. McKesson claimed that he was able to obtain a soft abdomen, given the greatest co-operation, and other favourable conditions, in an ordinary abdominal case? If he (Dr. McKesson) was going to be operated upon, would he expect to have his own abdomen soft, say, under gas and oxygen alone?

Dr. McKESSON: I am willing to say this: that in a robust or alcoholic patient one cannot get with gas and oxygen the relaxation that is possible with chloroform or ether. But with careful work you can get sufficient relaxation to enable the surgeon to operate.

Dr. McMECHAN (Chairman) said that in dealing with anæsthetics, it had to be remembered that there were two groups: the nitrogen group and the hydrogen group. In order to have a good nitrogen anæsthesia, it was necessary to secure a soluble gas of the nitrogen group; in order to have a good hydrogen anæsthesia, one must have a highly soluble hydrogen gas or hydrogen liquid. In nitrous oxide there had been found a higher oxide of nitrogen which was excessively soluble in the blood-stream and admitted of an excellent form of anæsthesia. The scientific basis of secondary saturation was not altogether merely the securing of a more complete atmosphere of nitrous oxide in the lungs and tissues; it was also an elimination of the insoluble element which interfered with anæsthesia, namely, the last vestige of nitrogen in the apparatus, in the gas and in the patient's body. It was only under those conditions that one secured a percentage volume of nitrous oxide and a solubility which was compatible with the full scope and limitations of nitrous oxide as an anæsthetic agent. Of course nitrous oxide, carried to an extreme, might be an anæsthetic possessing great danger, but when one realized that in its technique of secondary saturation at most three breaths of 25, 50 or 100 per cent. oxygen completely re-established the respiratory function, one would hesitate to say that the respiratory centre was in an extreme state of depression. So far as the relaxation of the musculature was concerned, American surgeons were accepting the view that the recovery of the patient was the paramount issue. The type of recovery depended on the kind of anæsthesia. Those surgeons who were co-operating and were satisfied with a pure gas and oxygen technique, were the surgeons who were developing a finesse in the technique of their operations which encountered the least difficulty. Those surgeons were winning their way on the basis of their statistical results, which were considerably better than those of surgeons using other methods. Certain hospitals were accepting the newer method in preference to others because it was compatible with the system of American efficiency. By the use of pure gas oxygen it was quite possible for the same hospital, with the same number of beds, the same number of nurses, surgeons and anæsthetists, to do one-third more operations a year than by any other known form of anæsthesia.

Dr. F. E. SHIPWAY (President), on behalf of the Section, thanked Dr. McMechan for presiding and those who had read the papers and had taken part in the valuable discussion.

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Section of Balneology and Climatology.

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The "Rheumatic" Diathesis.

PRESIDENT'S ADDRESS.

By R. LLEWELLYN JONES LLEWELLYN, M.B.

FROM the dawn of Medicine, the Ultima Thule of the physician's endeavour has been to penetrate and lay bare the secret origins of disease. For then, as now, it was realized that *Ætiology* is the corner-stone of the Temple of Medicine, and well may we feel chastened when we reflect on the number of stones rejected.

But though vital, humoral, and solidist schools have passed into oblivion, the doctrine of diatheses seems destined to endure, founded as it is upon the sure and abiding truth that "all flesh is not the same kind of flesh."

How then did these eighteenth-century physicians arrive at their conception of diatheses? Of the proximate causes of disease they knew little. Bacteriology, physics, chemistry, biology, and pathology were still unborn. They were confronted by the same mysteries as we ourselves.

Heredity was the bed-rock of their doctrine, for, excluding Mendelism, they were familiar with its salient features, reversion, sex-linked inheritance, and so on. Aware too that inborn predispositions do not always breed true—that a diathesis may express itself in polymorphic guise. Also that many heritable disorders, latent at birth, and throughout infancy, usually evolve at different periods of life, differing for each. How avoid, then, the inference that such were the outcome of inborn proclivities or diatheses, the more so, seeing that inheritance and variation were a feature of all organic evolution?

Again, did not the phenomena of natural immunity to specific disorders and the varied individual reaction of those susceptible give sanction to their assumption? Did not animals and plants also show like difference? If the horse was prone to glanders, the ox was immune, even as some apple trees were prone to canker, some cereals to rust and others immune, while as to idiosyncrasies, these seemed to them the very summation of diathesis—of individuality gone rampant. We see, then, that these old physicians intuitively apprehended the fundamental unity of human, animal and plant life. Moreover, they had grasped this great truth: that despite her proverbial indifference to individuals Nature everywhere and in all her phases strives for individuality, that each of her works shall have an essence of its own. Feeling the need of a word to express this profound truth, they chose the term "diathesis," which ultimately is but a synonym for individuality. The need, if I may say so, is still with us. For though we look askance at the term, we nevertheless bow to the concept it enshrines. If we did otherwise it would be sheer apostasy—an abandonment of our faith in the principles of heredity and immunity, natural or acquired. More than that, it would be wilfully to shut our eyes to the meticulous individual distinctions afforded us by ultra-chemical or biologic tests, with their capacity for almost infinite differentiation.

We may say that the old diathetic physicians were dreamers—that they had no facts. But the mere accumulation of facts is not science. Science is our conception of the facts, the act of judgment, perhaps of imagination by which we link the unknown with the known. Of this true scientific insight they were assuredly not

destitute. Indeed, in some dim way they seemed to get a glimpse of the pathway along which the Mendelian concept of disease is leading us. For they also sought to arrive at a more natural or biological classification of disease through a study of its genetic origins or affinities.

DEFINITION OF DIATHESES.

In the "New English Dictionary" a "diathesis" signifies a "permanent (hereditary or acquired) condition of the body which renders it liable to certain diseases or affections: a constitutional predisposition or tendency." Now the "arthritic" was certainly one of the first so-called diatheses laid down by our predecessors; it included both "rheumatic" and gouty manifestations; and it is with the first of these that we purpose dealing.

What, then, is the nature of the *constitutional predisposition* which renders certain persons liable to "rheumatic" affections. To achieve even a glimpse of its probable nature, we must ever be mindful of Claude Bernard's dictum that "all the phenomena which make their appearance in a living being obey the same laws as those outside it." In other words, that "all the manifestations of life are composed of phenomena borrowed from the outer cosmic world," and he adds, "it is not by struggling against cosmic conditions that the organism develops and maintains its place; on the contrary, it is by an adaptation to, and agreement with these conditions."

Now, the power of adaptation to an ever-changing environment is one of the most remarkable endowments of the human organism. In normal persons the process of physiological adjustment to such contingencies ensues with a minimum of disturbance. But not so in the rheumatic subject, who, as the French put it, is *très barométrique*—abnormally sensitive to variations in cosmic conditions. He is ill-equipped, therefore, to withstand climatic vicissitudes, changes in temperature, humidity, barometric pressure, and so on. In short, his power of compensatory adaptation to such changes is deficient; what is the origin of this failure in adaptive capacity? For this is of the very essence of the rheumatic problem. It seems to point to some inborn flaw in the intermediary mechanism by and through which our ceaseless adaptations to climatic vicissitudes are achieved, in other words, some defect or imbalance of the endocrine-autonomic system. Let us then envisage the rheumatic subject from this standpoint, namely, as an organic unity under the play of cosmic forces, and as a living being, whose life is but a fragment of the total life of the Universe. To this end, let us trace the mode of evolution or manner in which the rheumatic diathesis slowly unfolds under the influence of factors which are evocative rather than causative.

ACUTE RHEUMATISM.

We may distinguish three phases: (1) Prodromal or pre-rheumatic, which forms, so to speak, the pathological groundwork of the disorder; (2) the "rheumatism of childhood"; (3) that of adolescents or adults. Of these the pre-rheumatic is perhaps the most interesting. For the morbid trend of children of rheumatic stock is displayed early. Often reddish or fair-haired, of delicate complexion, they are excitable, highly imaginative, readily fatigued, and liable to emotional crises, night terrors, athetotic movements, and also tetany. Their skin, usually dry, is subject to periodic sweating; while cold extremities, dead fingers, chilblains or even true Raynaud's disease attest their vasomotor instability. Their mucous membranes, too, participate, as shown by severe attacks of diarrhoea, mucous colitis, cyclical vomiting, asthma and migraine; these often alternate in kaleidoscopic fashion. To sum up, the essential attribute of these children of rheumatic stock is instability, for both in the mental and physical sphere their response to normal stimuli is excessive and frankly abnormal. To what may this failure in adaptive capacity be

referred? The instability of their skin functions supplies, I think, a clue. This is manifested by its vacillating blood-supply, its erratic sweat secretion, the often defective pigmentation, and deficiency of subcutaneous fat. For the maintenance of a normal temperature largely depends on due regulation of the skin blood-supply, its sweat secretion, and the amount and distribution of its pigment and fat. We see, then, how grave are the cutaneous disabilities of potential rheumatic children. Is it surprising that their temperature is often subnormal, and that they are very sensitive to weather changes? To what, then, may these vagaries be referred, if not to a state of endocrine autonomic imbalance? For we know that the skin functions and their correlated temperature control are regulated by a hormone mechanism in which thyroid, adrenals, and pituitary participate. In addition, the assumption of an inborn tendency to endocrine-autonomic imbalance may explain the retarded growth or arrest of development not uncommon in these children of rheumatic stock. For Sir Arthur Keith's studies lead him to infer that future research will reveal a *growth* mechanism presiding over the cutaneous functions concerned in temperature regulation and the deposition of pigment.

Now, in ascribing these peculiarities to endocrine-autonomic imbalance, I would remind you that the term "diathesis" merely implies a morbid potentiality—something dynamic rather than static. Now, just as in disease, we have a *vis medicatrix* seeking to secure a return to normal, so also, as Haldane suggests, must there be in the healthy body, a *vis directrix* whose office it is to maintain the normal—a controlling influence which regulates those ceaseless adaptations essential for the maintenance of bodily activities at a normal level despite an ever-changing environment. Here, I take it, lies the core of the "rheumatic" diathesis, an inherent deficiency in the power of organic regulation. For, granted that these children are victimized by an inborn tendency to endocrine-autonomic imbalance, it follows that their power of organic regulation or adaptation to environmental vicissitudes must be more or less impaired. Their latent tendency to imbalance may be evoked by cosmic external or internal factors, and the erratic response of their skin and mucous membranes is but evidence of their tendency to generalized dysfunction of the neuro-endocrine system.

RHEUMATISM OF CHILDHOOD.

Seeing how early in life these signs of instability emerge, is it not somewhat unwise to postpone our recognition of the diathesis until so-called "growing pains," recurring tonsillitis, or endocarditis, give it what we are pleased to term an authentic stamp. The more so, seeing that "rheumatic" phenomena in children are often afebrile—even carditis or endocarditis—so that none may know the hour of their inception. In spite of this ignorance we seemingly assume that their efflorescence marks some occult change—that the merely "unstable" child has changed into the "rheumatic" child. But a child can no more escape from his diathesis than he can from his temperament. The "rheumatic" child is still the unstable child. Why, then, assume that his ingrained pathologic habit of instability has vanished? May not his fleeting "growing pains," his transient erythemas, his choreic twitchings, and even his cardiac irregularities, be but the polymorphic expression of his inborn instability—his diathesis? The child indeed is still true to type. For if his infantile or pre-rheumatic vagaries have been of paroxysmal or periodic type, are not the clinical elements of what Cheadle termed "the rheumatic series" also discontinuous and definitely cyclical? Phases of relative immunity alternating with phases of susceptibility or, as I prefer to put it, phases of adaptation alternate with phases of maladaptation to those factors, cosmic or other, that evoke rheumatic manifestations.

RHEUMATISM OF ADOLESCENCE.

With the passing of puberty the diathesis undergoes further evolution, and therewith the clinical facies of acute rheumatism alters. Joint swellings become dominant, cardiac lesions relatively recessive, and the disorder more fulminant and pyrexial in character. Whence comes this change if not from the genital hormones that flood the circulation with the advent of puberty? Moreover, does not the clinical transmutation following their entry indicate how intimately interwoven are rheumatic phenomena with disturbances of the endocrine sympathetic system?

Take the temperature contrasts, rheumatism in childhood often apyrexial, in adolescence pyrexial, and even hyperpyrexial. Do not these differences point to some imbalance in the thyro-adrenal complex responsible for temperature control?

Again, take the articular contrasts; in childhood, seldom more than a transient puffiness or œdema of wrist, ankle or knee, such as might reasonably be referred to vasomotor and trophic disturbances of innervation. On the other hand, in older subjects, joint swellings with effusion are obtrusive features. Nevertheless, the difference between them is, I think, *quantitative* rather than qualitative. In other words, does not their migratory habit, their rhythmic swell and ebb and lack of residual change suggest some special mode of pathogeny?

Does not their invasion and re-invasion savour of the paroxysmal or periodic, and their symmetry—at least in the serial sense—suggest some central controlling mechanism. For these features are quite alien to streptococcal and other infective arthritides. Salicylates, too, in these are impotent; and, as Ivy Mackenzie observes, there is no instance of infection outside the protozoal group yielding to a drug of this kind.

Now, seeing that the efferent sympathetic fibres to a limb regulate the blood-supply of the skin and deeper structures and also the cutaneous secretion, is it not possible that instability in the exercise of this function might also occasion local vasomotor and secretory anomalies in the periarticular and synovial structures? Such might conceivably be due to the fact that the genital hormones exert their effect through the medium of other endocrines—notably the adrenal cortex. Now, we know how markedly the adrenals influence circulatory and secretory processes, and just as asthma will yield to adrenalin, so also will massive synovial effusion, even when of long standing.

CARDIAC LESIONS.

As to the cardiac lesions, it would seem, *prima facie*, improbable that their pathogeny should be fundamentally different from that of the arthritic and cutaneous lesions. Does not the transient character of the arthritic distinctly suggest that the cardiac also under favourable conditions would be more benign if not transient? For it is admitted that some cases showing irregularity, bruits, or even dilatation, do recover wholly. We see, then, that some cardiac lesions, like the arthritic, do end in resolution. Is not this a definite hint that the mode of pathogeny of rheumatic lesions, whether arthritic or cardiac, is fundamentally the same? But to this all important subject I shall allude later, and meanwhile I would emphasize the inter-relationships of acute rheumatism in all its phases with endocrine disorders. Thus the skin anomalies, the proneness to fatigue, subnormal temperature and tetany of the "rheumatic" child, point to thyro-parathyroid inadequacy. In addition, this tendency to tetany seems to run through the life history of the disorder as it crops up again in the acute rheumatism of older subjects. Hence, I incline to believe that acute rheumatism develops by preference on a subthyroidic substrate. Certain peculiarities favour the assumption. Thus, we know that goitre in a woman is often associated with subthyroidism. Now, if acute rheumatism occur in such a subject or her offspring, it often proves rebellious to salicylates, but relents if thyroid be superadded. Does not this suggest

that the non-response to salicylates is linked up in some obscure way with thyroid deficiency? Now, in contrast, acute rheumatism rarely, if ever, occurs during pregnancy, not even if a pre-existing cardiac lesion reveals the rheumatic trend. Is this immunity due to thyroid hypersecretion—a species of auto-thyroid therapy? For the immunity ceases with delivery, though acute rheumatism often develops after prolonged lactation, with its correlated tendency to hypothyroidism. Again, the rhythm of intermittent hydrarthrosis, too, is almost always broken by an intercurrent pregnancy, and the same is often true of migraine, asthma, Raynaud's disease and other paroxysmal neuroses. Now, all these disorders are apparently the outcome of vasomotor and secretory disturbances, and it is, I submit, somewhat striking that acute rheumatism, like these disorders, should rarely, if ever, occur during pregnancy. It seems to suggest that the joint swellings of acute rheumatism may also be the outcome of vasomotor and secretory anomalies of neuro-endocrine origin.

Again, French physicians insist that fleeting thyroid swelling often ensues at the onset of acute rheumatism. We might hear more of it but for the fact that there is no spontaneous pain, only objective tenderness. Besides, the thyroid swelling responds to salicylates more swiftly than the joint swellings. Given, then, a coincident sore throat, how easily might it be overlooked. I have known such thyroid swelling precede and co-exist with chorea in a young girl. Other points, too, favour the probability of a thyroid reaction occurring in acute rheumatism: (1) Graves's syndrome may arise directly out of a subacute thyroiditis thus installed; (2) the frequency of an antecedent history of acute rheumatism in the victims of Graves's disease is well known, and has been recently emphasized; (3) minor signs of hypothyroidism often become manifest during convalescence from acute rheumatism. It may sound paradoxical that acute rheumatism may predispose to Graves's disease, and on the other hand, be followed by hypothyroidism. But I may observe that it is by no means certain that Graves's disease is due to hyperthyroidism; some authorities hold that Graves's syndrome arises by preference on a hypothyroidic substrate, and I would maintain that the same holds good of acute rheumatism.

MUSCULAR RHEUMATISM.

Some maintain that muscular rheumatism is wholly distinct from acute rheumatism and gout. In view of our ignorance of the exact causation of all these three affections this seems a somewhat rash conclusion, more especially so, seeing that acute muscular may merge into acute articular rheumatism, while the alternations of gout with lumbago and sciatica are proverbial. These muscle syndromes, it is true, are usually distinct, and we would willingly, for convenience' sake, keep them so. But our passion for infinite subdivision must not blind us to the fact that, clinically, they do sometimes overlap. Nor must we forget that a diathesis may masquerade in polymorphic guise. I sometimes think that the rarity of gout is more apparent than real, and that, for some occult reason, it tends nowadays to affect muscles and nerve sheaths rather than joints. For certainly some obstinate examples of this nature defy salicylates but yield to colchicum.

Nevertheless, it is somewhat striking that muscular rheumatism in childhood and youth often blends with acute articular rheumatism, whilst in middle age its affinities are with gout. Does not this suggest some fundamental unity? Now, both rheumatic and gouty subjects alike are prone to paroxysmal neuroses and vasomotor instability. If the blood-supply of the muscle be diminished or obstructed, a state of painful spasm or cramp ensues. Therefore, in the light of their abrupt, painful onset, is it not possible that this is one of the factors that enter into the pathogeny of lumbago, torticollis, and the like?

RHEUMATOID OR ATROPHIC ARTHRITIS.

The term arthritis, as applied to this grave disorder, is a misnomer. It is rather a neuro-endocrine complex of tropho-neurosis, the salient feature of which is generalized tissue-atrophy, involving not only bone and cartilage, but all the component structures of the limb. It usually occurs in young women of arthritic stock. As Coates and Gordon observe, the frequency of an antecedent acute rheumatism is greater than can be accounted for by its general incidence in the population. But whether it be infections, repeated pregnancies, emotional shock, or what not, the inter-connecting link is, I feel sure, the state of hypothyroidism that such may induce. It is upon this subthyroidic substrate that the prodromata of rheumatoid arthritis arise, i.e., the local syncopes and asphyxias, tetany-like cramps, and so on. In their midst the spindle-joints appear and, like the vasomotor phenomena, wax and wane until eventually the recurring vascular spasms induce trophic change,—skin, bone and cartilage withering into the small end joint. The progress of the disease is definitely cyclical, and this and other features show the enduring nature of the diathesis. Thus, though she may never have suffered from acute rheumatism, the rheumatoid woman harks back to the rheumatic child. Thus, her skin, usually dry, is prone to periodic sweats and vasomotor crises; whilst undue liability to fatigue and a subnormal temperature are common, and bouts of asthma, migraine and mucous colitis, are of by no means rare occurrence.

Other affinities, too, emerge. Thus rheumatoid, like acute rheumatism, has associations with Graves's syndrome. In my experience, it is when the thyroid undergoes functional exhaustion—as shown by muscular cramps, vasomotor spasms, or solid œdema—that rheumatoid arthritis most often supervenes. For a similar reason, it sometimes follows thyroidectomy or X-ray treatment of Graves's disease. These sequences suggest that hypothyroidism favours the development of rheumatoid arthritis. In view of the inter-relationship of thyroid and pancreas, I may state that I have seen rheumatoid arthritis develop in sequence to an operation for acute pancreatitis. Again, pigmentary changes suggestive of adrenal implications are often present, whilst the close association of the disease with ovarian disturbances need not be emphasized. In short, in atrophic arthritis, the evidences of endocrine-autonomic imbalance are multiple and obtrusive, and their ætiologic significance, and alike the therapeutic indications they afford, cannot be over emphasized.

OSTEO-ARTHRITIS AND GOUT.

Why is it that women at or near the menopause so often drift into a state of osteo-arthritis: while men in the same decade so frequently develop gout? In women osteo-arthritis follows decline or withdrawal of ovarian and thyroid hormones, as shown by collateral signs of hypothyroidism and vasomotor instability. As to gout, I would remark that authorities hold that at forty years of age the thyroid begins to undergo senile atrophy. Now, just as the time of onset of the menopause varies in women, so also in men does a decline in sexual capacity ensue earlier in some than in others. Gouty men often show signs of premature senility and I incline to think that in them there occurs a premature diminution or withdrawal of the genital hormones. Coincidentally, too, they often manifest signs of hypothyroidism and vasomotor instability, and I suggest that, comparably with osteo-arthritis in women, a state of endocrine autonomic imbalance may be a determining factor in the onset of gout. I would remind you that that astute clinician, Goodhart, was much exercised by the frequency with which his middle-aged patients with gout gave a history of acute rheumatism in youth. Now, McCarrison and others emphasize the frequency with which hypothyroidism follows acute rheumatism. Having in view, therefore, the intimate interdependence of the thyroid and genital hormones, it is possible that the above-mentioned hypothyroidism may be a factor in determining a premature male

climacteric. Moreover, there are suggestive clinical affinities. Acute rheumatism, like gout, has its articular and ab-articular forms which in both may alternate. Rheumatism in childhood is often monarticular and so is gout, but both tend later to become polyarticular. The joint lesions in both tend to be paroxysmal and periodic and each has its so-called specific—salicylates and colchicum. But their temperature curves contrast strikingly. From being low or afebrile in childhood, the temperature in rheumatism after puberty becomes pyrexial or hyperpyrexial. The reverse obtains in gout. At first sthenic and pyrexial, as years pass, it tends to become asthenic and afebrile, and this is true even of acute gouty polyarthritis. Doubtless some profound significance attaches to these temperature contrasts, and did we only know their inward meaning it might go far to justify Goodhart's conclusion that the acute rheumatism of youth might, as years accumulate, be transposed into the key of gout. To sum up, I would suggest that (1) the various disorders I have discussed are but the polymorphic expression of the arthritic diathesis; (2) that in each and all there is an inborn tendency to endocrine-autonomic imbalance, through which the latent diathesis discloses its presence; (3) that the tendency of rheumatism to change its facies with the onset of puberty, the predilection of rheumatoid arthritis for the reproductive period, and of osteoarthritis and gout for the menopause, or pre-senile epoch, all suggest that the endocrine changes associated with them, account for the superficial diversity but fundamental unity of these affections; (4) that infections, if and when responsible, act not directly, but indirectly—the intermediary mechanism being some instability or defect of the neuro-endocrine system. At the same time, I submit that our etiologic concepts must enlarge and take cognisance also of cosmic and other factors, equally capable of evoking rheumatic phenomena.

SEASONAL INCIDENCE.

All biologic research accentuates the fact that an organism and its environment are one and indivisible—its life in reality, but the expression of ceaseless adaptations thereto. Does not the stately roll of the seasons leave its impress on all vital processes, and slowly but surely their inward biologic meaning is being disclosed?

Now, both here and in the United States, acute rheumatism tends to appear in late winter and early spring—a period of change with its call for adaptation. Thus, the blood-calcium and phosphate falls during winter to its ebb in spring, and rickets and tetany decline. There is evidence, too, that the thyroid iodine and even the hæmo-bactericidal power are at their ebb in spring. In short, the seasonal incidence of tetany coincides with a low level of the blood-calcium and the thyroid iodine, and, seeing that tetany is common in the goitrous, it is significant that this same period, spring, is the time at which fresh goitres arise and pre-existing goitres enlarge. Obviously, then, spring is a time of stress for the thyroid and its adnexa, precisely the period to evoke any latent tendency to endocrine-autonomic imbalance.

Now, rheumatic children are subject to tetany and also to sub-thyroidism; and there are some who hold that calcium deficiency is an etiologic factor in acute rheumatism. Does not this suggest that the spring incidence of acute rheumatism, like that of tetany, is linked up with the correlated low level of the blood-calcium and the thyroid iodine? Now, the summer rise in the blood-calcium and in the thyroid iodine implies an adequate response to solar stimuli. The skin being the transmitting medium, it is possible that their cutaneous disabilities may inhibit their response to the biologic action of light—such failure of adaptation presumably entailing a lag in the normal summer seasonal increase of blood-calcium and thyroid iodine. Taylor and Poulton note that the incidence of rheumatism goes up *pari passu* with a rising temperature and growing hours of sunshine, and to a certain extent with humidity and east winds, but is actually less in times of much

rainfall. This is interesting, seeing that rheumatic children are often non-pigmenters, viz., do not tan readily with sun exposure. Pigment acts as a screen, and, in addition, converts light into heat, which, when extreme, is sweated off. Hence, lack or deficiency of pigment implies difficulty or failure of adaptation to the two great cosmic forces, light and heat.

Leonard Hill reminds us that during the war persons on a protein-deficient diet developed cedemas, especially on parts exposed to light. Now, rheumatism being rife in children of the poor, whose diet is often ill-balanced or vitamin-deficient, how exclude the possibility that fleeting joint cedemas and erythemas in some of them may also be due to light sensitization?

Again, why is it that the porphyrins—normally found only in traces in the urine and faeces—occur in considerable excess in acute rheumatism, as in tuberculosis? For these porphyrins, when injected into mice, sensitize the mice to light. That such photo-sensitizing substances should occur in excess in acute rheumatism and that the incidence of the latter should increase with growing hours of sunshine, is I submit, a somewhat striking correlation. More interesting possibilities perhaps reside in the undue liability to fatigue of the rheumatic child. For such liability implies a risk of lactic acid retention, and its diffusion into the blood-stream. Some significance, then, may attach to Gideon Wells's statement that lactic acid is a photo-sensitizer. The same may account for Still's observation that excessive or prolonged sea-bathing seems to predispose to acute rheumatism. For here we have ideal conditions for sensitization owing to better transmission of sunlight and its intensification by radiation from the sea surface.

Nor should we forget that cattle fed on buckwheat, and horses fed on Swedish clover, become sensitized to light. Black animals escape, but not the white or part-coloured, which develop erythemas and cedemas over their unpigmented areas. It is quite possible, therefore, that some of the green food-stuffs we consume in summer may contain fluorescent or sensitizing substances. The origin of rheumatism in childhood being still a mystery such possibilities require consideration.

Rheumatoid arthritis and osteo-arthritis, so far as I know, show no tendency to seasonal incidence, but there is considerable evidence forthcoming to show that, as in rheumatism, calcium metabolism is deranged in both these disorders. The same is true of gout, which undeniably tends, like rheumatism, to appear in spring.

I will now discuss climatic vicissitudes, the traditional bane of the subjects of gout and rheumatism; this involves consideration of their oxidizing capacity.

THE OXIDATIVE FUNCTION.

Clinically there is much evidence that the oxidative function in rheumatic subjects is pitched—physiologically speaking, in a minor key—adequate perhaps, in an equable climate, but inadequate in a variable one. For, the sudden changes of a variable climate transcend the powers of adaptation of such patients. Hence, their life history is strewn with maladaptations to climatic vicissitudes, which is not surprising in view of their vasomotor and secretory instability. For the processes of tissue oxygenation are exquisitely conditioned by cosmic or physical factors constantly in operation. Haldane and Barcroft have shown that the oxygen supply of the blood to the tissues must be continually adapted to their varying needs, and, moreover, distributed at a certain partial pressure, which varies with barometric pressure and humidity. Nor is this all, for differences in temperature, and similarly factors within or outside the organism that promote acidosis, all affect the oxidative function. All these, moreover, may affect the oxidation of the body as a whole or regionally, according as the various factors operate generally or locally.

In light of these findings, the vagaries—climatic and other—of the rheumatic subject, seem shorn, in part, of their mystery. For all these processes are essentially adaptive, calling minute by minute for regulation of the supply and distribution

of oxygen to the tissues. Again, seeing how multiple are the necessary adaptations, we realize how multiple also are the ways in which failure of adjustment may occur and in which rheumatic states may ensue.

For it is obvious that the inborn tendency of rheumatic subjects to circulatory or vasomotor imbalance must cripple their power of regulating the supply and distribution of oxygen to the tissues. It may be, too, that they labour under further disabilities. For the affinity of hæmoglobin for oxygen varies in different species. Human blood has a lesser affinity than cat's, and dog's blood than that of the horse. Even in animals of the same species, individual differences obtain, for apparently no two samples of blood, whether of man or beast, have the same dissociation curve. It may be, then, that rheumatic subjects constitute a group whose hæmoglobin shows a lesser affinity for oxygen, and moreover, that—as judged by the dissociation curve—the units of the rheumatic group may show individual differences in this vital process of cell-metabolism. In but too many, the actual oxygen intake may be impaired owing to cardio-respiratory inefficiency.

We see, then, why some climates benefit rheumatism, and others not, for it is always the individual's oxidative faculty that determines his manner of response. Hence it is that some patients do well at high altitudes—in spite of lowered pressure and diminished saturation of their hæmoglobin with oxygen. For their heart, lungs, and blood-forming tissues are equal to the strain of adaptation. Others lacking these reserves, do better at lower levels, their hæmoglobin being more saturated by reason of the correlated higher pressure. But vigorous and feeble alike fare badly if wide fluctuations in temperature, humidity, and pressure obtain: this is not surprising in view of the multiple adaptations entailed.

Thus, cold lowers the dissociation curve of oxy-hæmoglobin and less oxygen passes to the tissues, whilst heat raises it with increased transport thereto. Again at high pressures, the affinity of hæmoglobin for oxygen is enhanced, at lower pressures it is diminished. As to humidity, the diffusion inwards of oxygen depends on a normal degree of moisture in the alveolar air. Excess retards the oxygen intake, and deficiency hastens it.

In view of these findings, we see why sudden weather changes evoke vague pains, bouts of lumbago, pleurodynia, or exacerbations of arthritis, all of them signs of their diathetic taint,—their tendency to suboxidation. Since the effect of these cosmic factors on oxidative processes may be either regional or systemic, we are enabled to discern, to some extent, why some types of rheumatism are localized and others generalized.

MUSCULAR RHEUMATISM.

Why is it that some persons are so liable to muscular, as opposed to articular rheumatism? It seems to point to local controlling factors. Is it that the alkaline buffer constituents of their muscles—bicarbonate, phosphate and sodium protein—are inadequate? For A. V. Hill finds that the ability of a muscle to tolerate hard exercise and high lactic acid concentrations depends on the amount and efficiency of its buffers? Or is it that their muscles are lacking or deficient in glutathione and other oxidative catalysts—shown by Hopkins and Meyerhof to be present in muscles? Inborn deficiencies of this nature would clearly predispose the victim to muscular rheumatism. For *ipso facto* such muscles would be less tolerant of exercise and lactic acid retention and less capable of oxidizing the same. Given a deficient oxidative faculty one might expect that rheumatism would show a predilection for the muscles, seeing that these structures are so largely responsible for carbohydrate oxidation.

As to the abrupt painful onset, it is conceivable that exercise may evoke the latent tendency to vascular spasm which would further aggravate the tendency to suboxidation. Certain types of exercise seem more provocative. It is not when muscles are in rapid action that attacks supervene, but rather when, after being held

rigid in semi- or full-flexion an attempt at full extension is made. Now Lindhard's researches show that the blood-supply of the muscles held rigidly in flexion or semi-flexion is for the time being almost completely shut off. Consequently, lactic acid accumulates pending relaxation and restored oxygen supply. To sum up, given inborn lack or deficiency of muscle buffers or oxidative catalysts we see how readily muscular strain, a sudden drop in temperature or increased humidity, singly or in combination, may occasion outbreaks. For if the one promotes lactic acid formation, the others, by lowering the dissociation curve and oxygen intake, as well as by checking sweating and evaporation, retard its necessary oxidation and elimination.

RHEUMATISM IN CHILDHOOD.

Let us now consider the child of rheumatic stock in respect of his oxidative faculty. As already noted, vasomotor ataxia, undue liability to fatigue, subnormal temperature, and often persistent anemia, are striking features of the potentially rheumatic and often subthyroidic child. These peculiarities antedate rheumatic symptoms, and collectively bespeak a deficient oxidative faculty. Subthyroidism signifies suboxidation, and vasomotor instability implies irregularity in the supply and distribution of oxygen to the tissues. Now, we know that factors promoting acidosis throw strain upon the oxidizing capacity. If so, the marked liability of rheumatic children to recurrent vomiting or bilious attacks with their associated tendency to acidosis, may be of etiologic import. For such may merge without break into acute rheumatism; moreover, in the prodromal stages of recurrent vomiting, choreic movements, and a tendency to general restlessness have been observed. Thus, Sellards finds a significant degree of acidosis in acute rheumatism, as judged by the soda tolerance test, and Frothingham and Walker the same, as indicated by the CO_2 tension of the alveolar air. Again, Marriott and Howland, in the case of acidosis of children, find increased soda tolerance and diminished tension of CO_2 in the alveolar air. Now, our ignorance of the factors determining the onset of rheumatism in childhood is such that we cannot afford to dismiss flippantly so-called "bilious attacks" in these children. For vomiting, white stools, offensive breath, and a change in complexion, with drowsiness and sighing respirations, imply in children, not only a danger of acidosis but possibly an outbreak of rheumatism, or a recrudescence of it when already established. Diarrhoea, when present, accentuates the danger of acidosis, and a prompt resort to a mercurial purge with alkalies is indicated, especially if the urine contains abnormal acids—the more so, in that, if rheumatism ensues, we have the further danger that salicylates inadequately guarded by alkalies may produce acute acidosis. As acidosis is due to defective oxidation of the organic acids produced in metabolism, I submit that the abnormal liability of these children to so-called bilious attacks points to an inborn defective oxidative faculty. Living on the edge, so to speak, of acidosis, their diet should be well-balanced, seeing that not only carbohydrate deficiency, but even a sudden change in diet, or mere fright, may occasion the acidosis. For, just as a food acidosis may determine the onset of rheumatism, so also, I believe, will a fatigue acidosis.

FATIGUE AS A FACTOR.

Seeing that "rheumatism in childhood" is primarily not an affection of joints, but of the musculature, both cardiac and somatic, this predilection may be of etiologic import. For we are apt to forget that the primary symptoms in acute rheumatism are often located in the muscles. Like others, I have seen acute torticollis merge into acute rheumatism with endocarditis. Again, a child with so-called "growing pains" develops endocarditis, and in his leg muscles are found recent and tender infiltrations.

In the light of A. V. Hill's researches on fatigue, it is conceivable that the primary departure from the normal in some cases, at any rate, may occur in muscles. For, as he points out, lactic acid is present in the blood during and after exercise. If the exercise is prolonged it accumulates, and only with its termination is it

oxidized by the increased oxygen intake that ensues when at rest. But the speed and efficiency of recovery from fatigue are limited by two factors, the capacity of heart and lungs as regards oxygen intake, and, secondly, the local supply of blood to the somatic muscles actually involved, as well as the efficiency of the coronary circulation.

Now, as already pointed out, in these children the threshold of fatigue is lowered, and the swiftness of its induction shows that their power of oxidizing lactic acid is defective. In other words, they readily incur oxygen debt, and their rate and efficiency of recovery from fatigue are lowered. This is not surprising, in view of their thyroid deficiency, which in itself implies suboxidation. Hence, they are bad subjects for fatigue, and what for a normal child spells fatigue, in their case spells over-fatigue.

All admit that in older subjects, over-fatigue, with or without exposure to cold, is the common determinant of acute rheumatism, and I am inclined to think that that is so also in the rheumatism of childhood and especially of cardiac trouble. As to temperature, extremes either way are bad. Each patient calls for adaptation, as to which is their weak spot. I have known a boy, after bathing in a warm swimming bath, develop endocarditis within forty-eight hours. Also, I have seen recrudescences of rheumatism and endocarditis ensue immediately after immersion in warm baths. On the other hand, the same sequels frequently occur after prolonged or excessive sea bathing. But, I do not think this question of an antecedent fatigue has been sufficiently emphasized in view of its possible bearing on the ætiology of subsequent cardiac lesions.

As to the insidious onset of cardiac rheumatism in children, I believe the initial process is one of *malnutrition of the cardiac wall*, in the production of which certain possibilities may be advanced. As A. V. Hill points out, an efficient coronary blood supply is essential for normal recovery from fatigue. Is it not conceivable, then, that their general tendency to vasomotor ataxia or instability may involve the peripheral arterioles of the cardiac wall, all the more so, considering their tendency to asthma and mucous colitis? If the lung and intestine are not immune, then why should the heart be spared? Now, the fibroses in myocarditis are usually discrete, lying close to an arteriole the lumen of which may be blocked or narrowed by thrombi. Might not multiple and recurrent spasms of the coronary arterioles, even though fleeting, lead to tissue autolysis with resultant fibroses? For autolysis ensues much more rapidly in unstriated than in striated muscles. Again, such states of local stasis and asphyxia entail increased H-ion concentration, which markedly promotes tissue autolysis. Fortunately, serum, through its buffer function, tends to inhibit autolysis, and so with the restoration of a free circulation the morbid process ceases. Such might well be the explanation of these cases marked by arrhythmia, bruits, and even dilatation, which undoubtedly, like the arthritic lesions, undergo resolution.

Other factors may, however, intrude. Thus the heart in animals on a de-vitaminized diet undergoes structural changes—such as atrophy, lack of tone, with a tendency to dilatation, and, in some, local degenerative foci. Lastly, being often subthyroidic, the heart, as Falta points out, may share the infiltration found in other tissues in hypothyroidism.

Given such insidious undermining of the nutrition of the cardiac wall, it follows that dilatation may readily be induced by apparently trivial exertion. If such dilatation occur, the cardio-respiratory efficiency is, in consequence, correspondingly impaired. Hence, *ipso facto*, the induction of fatigue will be more speedy, and recovery from it more tardy and incomplete. In short, a vicious circle is established as the fatigue threshold sinks lower and lower with each recurrency of carditis or endocarditis. In other words, we are faced with a child whose oxidative metabolic faculty is progressively dwindling as his cardio-respiratory capacity continuously drops to a lower level with each successive attack.

I submit, then, the following conclusions: (1) That the insidious onset and often

afebrile course of cardiac rheumatism, and, similarly, the site and character of the muscular and fibro-muscular lesions, are compatible with their metabolic and non-infective origin; (2) that the primary change is one of cardiac malnutrition arising on a subthyroidic substrate, reinforced by a vitamin-deficient diet and recurring vascular stases in the coronary arterioles; (3) that fatigue is the prime determinant of initial and recurrent attacks of carditis and endocarditis, as the subthyroidism and assumed instability of the coronary circulation preclude speedy and efficient oxidation of lactic acid and other fatigue products elaborated during cardiac activities.

✓ In this connexion, it is interesting to recall that in endocarditis lenta the most frequent antecedent is prolonged over-exertion, and Carey Coombs reminds us that Walker Hall's researches suggest that lactic acid favours the growth of low-grade organisms. It may be that bacteria found *in situ* in rheumatic endocarditis are of the nature of epiphenomena.

In the light of A. V. Hill's researches, the old lactic acid theory may undergo revival in modified form. It was abandoned largely because lactic acid was thought to be so swiftly oxidized that it could not possibly be responsible for a disease of often weeks' duration. That this is so in normal subjects is true. But as Hill clearly shows, the speed and efficiency of its disposal depend on the cardio-respiratory efficiency. His researches were carried out in athletes, but as he says:—

"the same degree of exhaustion may be produced by a much lower level of exercise, no more rapidly, but just as effectively in a person of lower oxidative faculty or with poorer buffers in his tissues."

In older subjects, the most common determinant is over-fatigue, the disorder ensuing in a few hours or in one to two days. In such cases it is well to remember that the initial depression of the circulation through muscular exhaustion is increased by the acidæmia, which further lowers the blood-pressure. This, moreover, is aggravated by the incidental augmented transudation from the blood-vessels, with consequent capillary polycythæmia. In short, a vicious circle is produced; the capillary obstruction tending to prevent the oxygenation of the muscles, which of course aggravates their asphyxial condition, with further production of lactic acid and consequent acidosis and acidæmia.

In view of these sources of delayed oxidation, we see that one of the main objections to the lactic acid theory is minimized—the swiftness of its oxidation is only conditional. For, obviously, it may be otherwise, seeing that it is not only a question of lactic acid in the blood but of the accumulation of acid products and diminished alkalinity in the muscle tissues. Consequently, we may be dealing with recurring states of acidæmia, as the circulation washes successive amounts of lactic acid into the blood-stream.

We know that Richardson produced endocarditis and migratory arthritis in dogs by injecting lactic acid into their peritoneal cavities, and also that Foster repeatedly induced an arthritis of similar character in a diabetic undergoing lactic acid treatment. It is true that the lactic acid used was lævo-rotary, whereas its optical isomer—sarco-lactic acid—is dextro-rotary. It seems certain that the former, if injected, can produce a fleeting arthritis, but as far as I know, no investigations of sarco-lactic acid from this standpoint have been undertaken.

Pending further research, we must therefore rest on the assurance that muscular exhaustion induces acidosis and acidæmia, and that these conditions exist in cases of acute rheumatism preceded by over-fatigue. Whether these, of themselves, would be adequate to produce the disorder in persons of a rheumatic diathesis, or whether they are only contributory factors, must remain for the present uncertain.

RHEUMATOID ARTHRITIS, OSTEO-ARTHRITIS AND GOUT.

The same factors promoting suboxidation are present in all three of these affections, viz., hypothyroidism and vasomotor instability. Again, both in rheumatoid arthritis and osteo-arthritis, basal metabolism is more often below than above normal, whilst the frequency in their instance, and also in that of gout, of lowered sugar tolerance betrays their feeble oxidizing power. The striking benefit of a restricted food intake is a case in point; this is a blessing which sometimes comes in disguise. An acute illness or an operation entails modified starvation, and the joints markedly improve, but unhappily only to relapse when their food intake transcends their oxidizing capacity. In short, in the case of these arthritides, we have either to restrict food intake, or augment the metabolic output. The ideal aim of both is the same, to correct the inherent tendency to suboxidation. But our most effective procedures are such as stimulate body metabolism, namely, climatotherapy, hydrotherapy, and massage.

How, then, link up these tendencies to suboxidation with their inborn proclivity to endocrine-autonomic imbalance? We know that the phenomena of diabetes have been traced to the deficient functioning of certain cell groups—the pancreatic islets. Is it not possible, then, that the varied manifestations of the rheumatic diathesis may be traced to some lack or deficiency of those oxidative catalysts, known to be elaborated by the endocrine organs and other tissues? Thus, recent researches at the Mayo Clinic have shown that the processes of tissue oxidation are greatly influenced by the thyroxin molecule, and that the epinephrin of the adrenals also acts as an oxidative catalyst. Apart from its influence on the respiratory exchanges, the thyroid, through its interaction with the adrenals, regulates blood-pressure, and the supply and distribution of oxygen to the tissues. Also, through the medium of the pancreas and adrenals, it regulates carbohydrate and calcium metabolism, and to a large extent the body temperature. Moreover, the gland itself is as sensitive to lack of oxygen as it is to lack of iodine, and very sensitive also to cosmic factors, notably barometric variations. Lastly, it reacts swiftly to infections, food deficiencies, and psychic influences.

In the light of these data, is it not possible that the deficient power of "organic regulation" in "rheumatic" subjects—of ceaseless adaptations in the supply and distribution of oxygen to the tissues, may hark back to some inherent defect or instability in the endocrine-sympathetic system? Instability rather than deficiency is, I think, more distinctive of "rheumatic" subjects, for though their primary trend is in the direction of endocrine deficiency—notably, but not exclusively of the thyroid, nevertheless, there is always a striving after endocrine equilibrium. Hence, we often see, both in the rheumatism of childhood, and also in rheumatoid arthritis, signs of hypothyroidism associated with those of hyperthyroidism. In short, we see that many of the peculiarities of the so-called rheumatic diathesis may conceivably be the outcome of defective functioning of the endocrine-sympathetic system, with its correlated tendency to suboxidation. ✓

THE RELATIONSHIP OF GOITRE AND OF EXOPHTHALMIC GOITRE TO "RHEUMATIC" DISORDERS.

There is a tradition that both "rheumatic" disorders and goitre are the outcome of certain *cosmo-telluric* conditions. Both, too, were regarded by our predecessors as diathetic diseases, and certain other broad generalizations obtain in regard to them. Thus, goitre affects, predominantly, *females*, and recent studies show that the same is true of "rheumatic" disorders. Again, the periods of increased incidence of rheumatic disorders synchronize markedly with puberty, the child-bearing period, and the menopause—the precise periods, too, at which new goitres

arise, pre-existing goitres enlarge, or at the menopause undergo involution. Also, prior to the advent of salicylates, iodine and the iodides were the sheet-anchor in treatment of both rheumatic disorders and goitre.

With regard to telluric conditions, it may be said that rheumatism is ubiquitous, but the same holds good also of goitre, for its endemicity is purely relative. Nevertheless, it is unquestionably true that both are much more prevalent in some regions than others. Thus, the incidence of goitre is abnormally high in marshy, alluvial districts, along the banks of rivers, canals, and the shores of estuaries, and the incidence of rheumatic disorders in such low-lying districts is equally high. Again, the recent Report of the Health Ministry reveals that the incidence of, and mortality from, acute and cardiac rheumatism, is markedly higher in regions where goitre is endemic than in those where the question of its endemicity has not arisen, and the same holds good with the incidence of rheumatoid arthritis and osteoarthritis. Also, it appears from Campbell's analysis of the Registrar-General's statistics that the mortality from exophthalmic goitre is also generally much higher in regions where goitre is endemic, and the incidence and mortality from rheumatic disorders are correspondingly high.

Reverting to endemic goitre, the significance of its geographical coincidence with rheumatic disorders is distinctly enhanced by the fact that not only do goitre and rheumatic disorders arise under the same cosmo-telluric conditions, but that the two affections frequently co-exist in the same individual. This seems to point to a common ætiologic factor. In addition, the sequence is usually goitre and then some rheumatic or rheumatoid affection; this suggests that goitre or thyroid inadequacy may be the medium by and through which the rheumatic diathesis finds expression. For goitre is frequently associated with thyroid instability—with a dominant bias towards hypothyroidism. Now, hypothyroidism, as already stated, renders the victim abnormally sensitive to climatic vicissitudes, and his maladaptation to these betrays itself in rheumatic manifestations.

It is important to note that it is not goitre but the correlated hypothyroidism that predisposes the victim to rheumatism. For though goitre itself may not be hereditary, the frequently associated thyroid instability or hypothyroidism is distinctly so. Hypothyroidic women bear hypothyroidic children; which in view of the hereditary and familial tendency to acute rheumatism is interesting. For it suggests that the transmission of the rheumatic tendency may be by way of the endocrines; in other words, that the hypothyroidic merges into or is identical with the arthritic diathesis.

Where goitre abounds, states of thyroid inadequacy or instability will necessarily be more common; this may account for the excessive prevalence of rheumatic disorders in goitrous regions. The incidence of rheumatism in non-goitrous regions does not negative this assumption, since that thyroid inadequacy or instability more often than not exists without any enlargement.

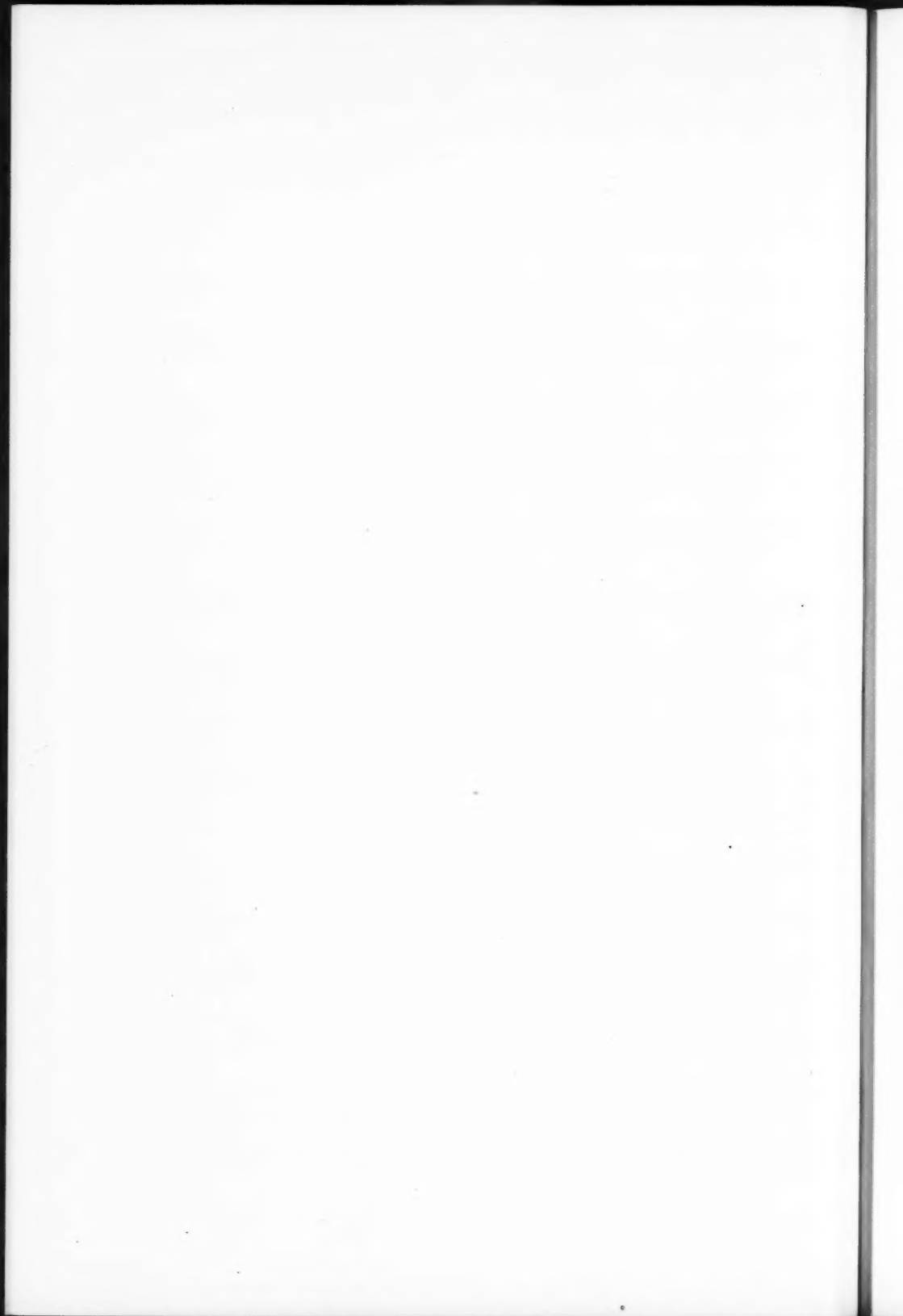
In seeking to emphasize my contention that hypothyroidism predisposes to rheumatic disorders, I would point out that Albert Kocher is so convinced that hypothyroidism predisposes to rheumatism and heart trouble that he suggests treatment with thyroid grafts. The same inference may be drawn from Deaver's experience of partial thyroidectomy in Graves's disease. He states that after this operation the victim's resistance to rheumatism and endocarditis is lowered.

As to the relationship of endemic goitre to rheumatoid and osteo-arthritis McCarrison states that the frequency with which the two conditions co-exist in the Himalayas, is such as to suggest a similarity of origin. Again, Mutch, in discussing 200 cases of chronic arthritis observes :

"In this series, minor forms of hypothyroidism were very common, while well defined myxœdema or goitres of considerable size were seen in 14 per cent. of the cases."

In conclusion, the evidence that endocrine and rheumatic disorders are intimately interwoven is, I submit, cumulative; reinforced as it is in the sphere of therapy. Have we not from time immemorial prescribed iodine or the iodides for both goitre and rheumatic disorders? The good results may possibly have been due to the fact that we were unwittingly correcting the underlying thyroid inadequacy. Again, do we not to-day, in both complaints, invoke thyroid therapy, intestinal antiseptics and often change of residence or water supply? Seeing that goitre and rheumatic disorders overlap not only clinically but geographically, it seems at least possible that the aetiological factors responsible for their production likewise overlap or are perhaps identical. It may be, then, that the fundamental predisposing factors that promote the development of "rheumatic disorders" ought to be sought for in those conditions—extrinsic and intrinsic—that favour the genesis of goitre or, to speak more exactly, "thyroid instability" or inadequacy.

To sum up, it would seem that our views as to the nature of this great mysterious disease—rheumatism—must become more catholic. For its pathogeny cannot be pent up within the narrow compass of a septic tooth or a decadent tonsil. Not that either of these should be disregarded, but each viewed in its proper perspective, as not the sole cause, but merely as one of the constellation of factors, cosmic and other, that bring to light the latent morbid potentiality—the diathesis.



Section of Balneology and Climatology.

President—Dr. R. LLEWELLYN JONES LLEWELLYN.

Airs, Waters and Places.

By F. G. CROOKSHANK, M.D., F.R.C.P.

IT will not, I think, be disputed by those who are interested in Hydrology, in Balneology, in Climatology, and in allied branches of medicine, that two tendencies have lately become manifest at places where what is called spa treatment is carried out. The one is to explain (as it is said) the benefits accruing from treatment at any particular spa, in terms of ions, electrons, radio-activity and other fashionable fictions of the physico-chemists: the other, for particular spas, of malice aforethought, to abandon, submerge or lose their particularities, their individualities, and their character, in a competitive struggle for commercial success.

The prophets of Israel, no longer content with enjoining their clients to bathe seven times and be healed, now supply doubting Naamans with professedly rational explanations of the cure that is about to take place, and, no longer content with insisting that the waters of Jordan-les-Bains are really more efficacious than those of Abana and Pharpar, take pains to advertise the fact that their progressive municipality has recently installed sumptuous apartments where Abana douches, Pharpar wash-outs and Egyptian coloured lights may be administered in accordance with the directions of the priests of the House of Rimmon.

At any rate, both these tendencies—the tendency to afford “scientific” explanations of the inexplicable, and the tendency to set up artificial substitutes for what is only successful when natural—are the outcome of the notion that it is the mission of science to explain to us what happens in the outside world. Unfortunately, adherence to this doctrine leads many doctors to refuse belief in the occurrence of what they cannot at once explain in terms of current science—so that they are compelled, either to remain sceptical, or to invent some form of words that leads them to think that they *do* understand the workings of the natural world and can even imitate the processes of Nature in all their mystery.

Of course science never did and never will explain aught about anything in the way that once, when medical students, we thought it did. All science can do is to provide us with general statements that are convenient summaries of experience, that lead us on to make fresh observations, that so enlarge our experiences, and amplify our practical resources. At most, science “explains” by referring one set of phenomena to the generalization or law assumed in respect of some other sets of phenomena. But of the attempts to afford ultimate explanations, and of the assertions made concerning “modes of action,” causation, and the like, by those who use these terms so glibly, the less said the better.

Now, in any text-book of medicine written towards the end of the last century, in those wonderful days when we thought Darwinism had taught us how man came to be, and that physics would shortly let us know all about the universe,—any text-book of medicine, I say, written when we thought that the stethoscope and the post-mortem room, with the aid of the microscope, would teach us all we need know about life and death and disease—spa treatment was only mentioned in terms of depreciation with hints about a “pervading atmosphere of quackery,” and gentle gibes, like those of Sir Clifford Allbutt, about people who believed in the efficacy of the “water

chemicals." This sort of scepticism was natural enough to physicians who really did refuse belief in what they could not, as they said, "understand," and who, at the time of which I speak, deemed disease itself to be a kind of parasite that invaded particular organs, or later, pictured the world of disease as populated by armies of specific organisms going about seeking whom they might devour.

These views have so impressed themselves upon the profession that it will be a difficult struggle before what I may call the functional view-point is re-established, and we come to see that the greater number of diseased states, so far as they are of bacteriological origin, are reactions between the body of the host and organisms which normally are harmless (if not necessary), but which turn "bolshhevik" and become mischievous when the functional integrity of the host weakens or is perverted. Be this as it may, however, it is a fact that since the time of which I speak, medical men, not content with observing the benefits accruing from spa treatment simply, naturally and conscientiously carried out, have seemed to derive some kind of satisfaction from alleging these benefits to arise from radio-activity and what not; as if such alleged explanations made the matter any more clear! Of course they do not. In the words of a well-known stage gag, they make it more difficult! We are indeed no nearer the ultimate understanding of the curative processes initiated at Bath or Harrogate than we were a hundred years ago, when crude chemical analyses were first put forward as explanations. Perhaps we are no nearer than we were 2,000 years ago when the Romans invoked tutelary deities! But the empirical observations are as true as ever! Even if we say that the sceptics who declare the whole effect of spa treatment to be "psychological" are right, what is gained? Are the results any the less valuable and desirable? Is the *modus operandi* any more clear? Suppose that at Bladudville (where, as Mr. Bernard Shaw has discovered, chronic inflammation of the nuchal sac speedily disappears), we find that the waters contain distinct traces of lunar emanations in solution. Do we really understand better than before why and how people afflicted in their nuchal sacs get better at Bladudville? All we have done, even when we find that lunar emanations in solution elsewhere, go hand-in-hand with apparent cures of nuchal sac disease, is to establish a correlation and to shift the credit from the waters of Bladudville to solutions of lunar emanations. But why and how do these cure? It is the shift from the familiar to the unfamiliar that, in an American phrase, makes us "feel good," and that we have really found out something. In the meantime—if analogy counts for anything—we have probably lost a good deal more. Consider our experiences with quinine. A hundred years ago we had accumulated a vast store of experience concerning the cinchona bark, and its virtues were extolled, even in heart disease. Then came a time when chemistry foisted quinine upon us, and we laughed at those who thought bark was a cardiac tonic. We now give the once despised and rejected quinidine with amazing success not only in cases of heart disease, but in certain malarial fevers. Did we not then lose something when, in a moment of arrogance, we scrapped all that 200 years of clinical observation had taught us about "the bark"? And so, perhaps, is it in respect of our latest and supposedly most scientific "explanations" on physico-chemical lines concerning what happens at spas. There is the danger of diverting attention from sequences of experience, from clinical happenings of importance that should be observed and pondered, but which are dismissed, because the latest shibboleths offer "no explanation." As Mr. Bertrand Russell has somewhere said, and with profound truth, "there is nothing in the whole universe really less understood than why one billiard-ball rolls on when struck by another." And there is no quackery to-day more dangerous than the verbal quackery which, flourishing as luxuriantly in Harley Street as at any spa, allows us to pretend that we are nearer the ultimate understanding of life, death and disease than was Hippocrates: renders us content with the barren stone of false explanations instead of the bread of experience; and induces us to participate in an

attempt to standardize, to industrialize, to commercialize, Nature's own methods of cure, or rather to provide in the shopman's phrase: "Something which is quite as good"—but which is not!

Now the proposition that I would make is one that seems to me to embody a conception of which we are in danger of losing sight; and it is this: that the advantages derived from treatment or residence at any spa, in like manner to the physical and psychical consequences of birth and life in particular regions, are not fairly to be attributed to any isolated factor, but are a function of the *milieu*—in the sense of Auguste Comte. That is to say, they are a function of a totality of exterior circumstances necessary to provoke the characteristic reaction on the part of the individual.

As a matter of fact, the essential truth of this notion (which is, of course, in essence, synthetic rather than analytic) is implicit in two old and well-established aphorisms: the one that when at Rome we should do as the Romans; the other that when abroad we should drink the wine of the country. And I think that if we pay attention to this point of view we appreciate much that seems at first sight improbable, and we save ourselves much fruitless effort in straining after scientific rainbows. For, once relieved of the necessity of being incredulous as to the truth of what we do not understand, we waste no time in groping after explanations that explain nothing, and we find opened up before us a whole entrancing field of empirical observation that has been for long closed to those who are afraid of being labelled empiricists, if they observe without theory, and theorists if what they observe is inconsistent with dogma. We have been far too long under the tyranny of the laboratory theorists who declare that only in a laboratory can experience be gained. Experience in the field is every whit as truly "experimental" as is experience in the laboratory, and, for the physician and epidemiologist, more directly relevant. Yet such is the craze for analogical observation in the laboratory that even epidemiology—the science of disease amongst communities—is now being reduced to an affair of mouse traps.

Indeed, if we wish truly to progress, we must get back—and the sooner the better—to Hippocrates, whose empirical observations and whose few, yet grandly simple synthetic generalizations and inductions remain, and must ever remain, the foundation of all true medicine based upon the observation and study of Nature, of Nature's ways, and of Nature's remedies.

Nowhere in the Hippocratic Corpus is the quality that we love to ascribe to Hippocrates better manifested than in the immortal work which we know as *Airs, Waters and Places*, to which I would now make some allusion, first premising that a strong current of thought has lately set in, avowedly based upon the Hippocratic doctrines. To-day in France a new school is engaged in building up a new science of morphology which has little to do with the old, or formal morphology of the Victorian or Darwinian era, but which considers human form as the expression of human function; of functional reaction to *milieu*, or environment. This school, now led by MacAuliffe, Arone, and Theoris, derives inspiration from the teaching of Sigaud, Vincent, and Giovanni, and I would remind you that it was Sigaud who achieved the best definition of disease yet formulated; namely, that disease is dissociation of the functional unity of the organism. The object of this school is, then, the study of Living Man: of Man reacting to external influences, and revealing his individuality in his method of reaction; not only in anatomical form but in temperament—that is, functionally, psychically, and chemically, as well as physically.

This new science of morphology, then, seeks to observe man not as a static thing, disjunctive to surroundings, which compel him to life or death as he is or is not fit to survive, but as constituting, with his surroundings, one definite continuity that exhibits a perpetual flux of adjustment and readjustment.

And this is what the *Airs, Waters and Places*—that marvellously concise summary of accurate observation expressed in generalized form—teaches us to do, at the same time that it gives us in outline the general theories of epidemiology, of climatology, of hydrology and of functional anthropology so set out that there is but little to be added. And, moreover, these theories are theories of the right sort: synthetic statements of the kind which Poincaré says the fruit of right generalization should ever be—synthetic statements which indicate belief in the essential simplicity and unity of that nature which, as Bordeu, the French Hippocrates, declared, is yet so much more profound than is the most sublime mathematician or physicist.

Unfortunately, almost without exception, every English translator of Hippocrates has thought fit to employ a peculiar jargon that, however useful to the Greek student, fails to convey, to those who are not classical scholars, the force and directness of the original. The French translation of Littré is, however, beautiful in itself, and may perhaps account for the greater appreciation shown in France for the Hippocratic teachings.

"In the beginning," says the ancient writer, "whoever would wish to pursue properly the science of medicine must in the first place consider the characteristic effects produced by the seasons of the years, remembering that not only does each season in any year differ from the others, but that the same seasons differ in successive years. And then the airs and winds; such qualities as are common to all countries and such as pertain to particular localities. And then the properties and qualities of waters; for, as these differ in their physical characters, so do they differ in their action upon the body. So, too, must be considered the situation of towns, with regard to the prevailing winds, and to the rising sun. And the waters used by the inhabitants: whether marshy and soft, or hard, and from rocks, or salt, and unfit for cooking. And the habits of the inhabitants: their avocations, and whether they be eaters and drinkers to excess and indolent; or industrious, vigorous, frugal, and abstemious. From these things must he proceed to investigate certain others in particular, so that, when he come into a strange city he will understand the diseases there endemic, and the modifications of common maladies that there obtain."

Later, after some further detailed discussion of airs and waters, the writer passes on to the enunciation of what is perhaps the most famous, though the most frequently ignored, observation in epidemiology; namely, that in respect of not only epidemic but other maladies, the most important and dangerous seasons of the year are those of the two solstices, especially the æstival; and the two equinoxes, especially the autumnal. Belief in the accuracy of this observation implies no credulous acceptance of astrology, but recognizes an empirical fact, as also the associated induction that fluctuations in weather as well as of health tend to occur at those periods when there is variation and change in the relation of the heavenly bodies amongst themselves and to us. Even modern science has not gone so far as to dispute the relationship between the spring time and germination or between autumn and the fall of the leaf! Moreover, we are gradually recognizing as a matter of fact that, not only is there a seasonal correlation in respect of influenza, poliomyelitis and encephalitis, but that there are seasonal fluctuations and variations in the incidence and exacerbations of duodenal ulcer and pernicious anæmia—explain them as we may—to say nothing of other diseases!

However—and this is what particularly interests us here to-day—the Hippocratic writer not only recognizes the correlation between seasons and times, and those disorders of adjustment to the environment that we call being ill, but a definite correlation between climates, the physical peculiarities of places, and types of mankind. And in the passages in which this view is stated may be found the chief tenets of the school of observation to which I have alluded, as well as what is the rational foundation of that branch of medicine which makes use of airs, waters, and places for orthopædic and therapeutic purposes.

"For," says Hippocrates, "where the seasonal variations are most abrupt, there also is the country the most diversified, and the wildest. But, where the seasonal changes are the

least marked, there is the countryside the most uniform. And so, when we inquire, is it found to be the case, even with the inhabitants. For as some physical natures are like to the well-wooded and watered landscapes where they occur, so are others to the thin and poor soils; and others again to arid, parched and barren fields, and others to lush meadows and pasturages."

Of course this is not merely fanciful, as we may be inclined at first blush to think. It embodies an anthropological fact well known to simple observers, even if hidden from the learned. Every schoolboy knows Charles Kingsley's description of Martin the fensman, and Scott never lost an opportunity of instituting comparison between the rugged Highlander and the mountains of Caledonia, stern and wild. Now MacAuliffe and his colleagues have drawn attention to the fact that we can trace, cutting right across all other differentiae, the occurrence throughout the whole of the animal kingdom of distinct types, so that we have rounded, or (chemically) hydrophilous types of men, horses, dogs, and even fishes, as well as (chemically) anhydrophilous or linear types of men, horses, dogs and fishes. Similar distinctions have been made in respect even of the vegetable kingdom, so that the influence of environment is nowhere better displayed than when, in the arid and dry countries we find men, beasts, birds, and plants of one type, and *vice versa*.

For those who seek explanations of the usual kind, one may commend the work of Regnault, who, some years ago, definitely correlated the physical peculiarities of French peasants and agricultural labourers, in different regions, with the local peculiarities of the soil to which they are so much attached. Thus, in the quality of mineralization of the water, and so of the food, both vegetable and animal, in special districts, we are to see the explanation of the similar quality of mineralization, and so of physique, of the inhabitants. This question is intimately linked with that of the endocrine glands and their influence on physique, for we are becoming more and more recognisant of the fact that activity of the thyroid, for example, is linked up with iodine in the food and drink: that of the parathyroid with calcium and so on. We are only just beginning to nibble at this question, I say, but I venture to suggest that one of the advances of the future will be a recognition of the part played by minute traces of silicon, of fluorine, of arsenic, of copper and of other minerals in our food and drink, in their relation with the activities of particular glands and so in the production of physical and perhaps racial types, of one kind and another. At any rate, we are more and more driven to recognize that, as Regnault hinted, environment, while yet an *ensemble*, a unitary fact, is nevertheless of extreme complexity, its full appreciation involving perhaps a reconciliation of much that at present appears opposed in biological and anthropological thought. But these questions are no less complicated than are the epidemiological questions raised by the airs, waters and places, and it would seem that in both respects we are wiser men when, instead of spending time and energy in an endeavour to isolate this or that specific factor or to secure victory for this or that theory—Darwinism or Lamarckism, miasm or contagium, soil or seed—we seek to balance the results of modern and analytic methods by appeal to the older empiricism with its synthetic judgments and simplifying inductions.

It may be said, however, that Hippocrates does not, in the work to which I have alluded, make any express recommendations of a therapeutic order. True, but the therapeutic usage of airs, waters and places, so far as it is rational, is a direct outcome of the Hippocratic study of the influence of the *milieu* upon the health and character of the inhabitant. It certainly involves, I think, a greater recognition of the thought of Lamarck than it is usual to accord in this country: for, after all, when we send someone away to Bath, to Harrogate, or to the Pyrenees, for the benefit of their health, we are sending them away in order that they may be provoked by the new environment to respond, to adapt, to adjust, in a manner that we think desirable. That is to say, we do so if we are not ourselves misled, by our own jargon, to think

we are sending them away in order that some "specific" effect may be produced, by some specific form of electrical or lunar emanation. But if we hold to the Lamarckian philosophy and the Hippocratic tradition, we shall wonder whether the complexity of modern life and the luxuriant mechanisms of this age of gramophones, cocktails, wireless, evening papers and tinned foods, are not co-operating to destroy what we should earnestly wish to conserve—the local characteristic and individuality of these environments to which we resort. It seems to me that the local characters in respect of the airs, waters, foods, habits, and so forth, should be far more jealously guarded than they are. If we fail to remember, with Montesquieu and with Rousseau, that the peoples of this world are but as ant-swarms to whom the soil, the *milieu*, has given character, temperament, complexion, habits, form and function, and for whom climates and seasons, sounds and silence, colours, darkness and light, elements, aliments, movements and repose, have all contributed to produce the effects we observe as racial, temperamental, and personal characteristics, then we will find ourselves co-operating in the smoothing out of all those local characteristics, physical, dietetic, hydrological, balneological and the like, which have for centuries been recognized as beneficial, both in varieties of health and in varieties of disease. It is idle to attempt to enlist Nature in a partnership of which the *raison d'être* is the sophistication of Nature's methods. And I am not sure that even the spa physician himself is not more successful—in the right sense—when he, too, is a native and an inhabitant, with local colour and local tradition, rather than a fashionable and fugitive visitor during the high season.

At any rate, the more close is the link between the physicians and the locality, the more valuable will be their contributions to epidemiology and to our knowledge of the play between airs, waters and places and states of health and disease. We do more and more need observations of such nature as only the cultivated physician, attached to the soil and observant of Nature and Nature's methods can give us. Your President himself, with his important and valuable observations on the relation between rheumatism, temperaments, and the soil, has abundantly illustrated my meaning. Surely, if ever, the riddle of rheumatism will be solved by the co-ordination of such observations as those of Dr. Llewellyn with laboratory work, rather than by laboratory work alone.

The laboratory *by itself*, is bound to fail. But there is no reason why we should not prosecute investigations in the laboratory side by side with observation in the field of Nature: no reason perhaps but this, that, when we do prosecute observation in the field of Nature we are not quite so confident of attaining ultimate explanations as are our valued colleagues of the laboratory! And, even if we are driven, like Hippocrates and like Sydenham, to invoke "occult" and "hidden" forces, that will not mean that we are falling back into superstition and into darkness. It will, on the contrary, perhaps mean that we are adopting a more truly philosophic and scientific attitude than are those who make glib use of the verbal "explanations" that pass current to-day, and that obscure, rather than indicate for us, the operations of Nature and our reactions to that Nature around us, of which we form part.

PROCEEDINGS
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AND
T. WATTS EDEN, M.D.

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THE EDITORIAL COMMITTEE

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SESSION 1925-26

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Clinical Section.

President—Dr. G. NEWTON PITT, O.B.E.

A Case of Aortic Disease in which relief from the Anginal Complex coincided with the onset of Auricular Fibrillation.

By B. T. PARSONS-SMITH, M.D.

W. H. W., MALE, aged 58. Attended hospital September, 1923, complaining of pain in the chest (the typical anginal syndrome—substernal pain, constrictive in type, induced by effort, relieved by rest), breathlessness and frequent attacks of bronchitis during the previous four years.

Past history.—Rheumatism at 28 years of age; enteric fever at 33; several attacks of bronchitis; has never been excessive as regards taking alcohol; a non-smoker.

Clinical findings.—Heart enlarged; apex beat in the sixth space 5 in. from the mid-line; rhythm regular except for occasional premature contractions; systolic and diastolic murmurs, also systolic thrill in aortic region; vessels thickened; blood-pressure 150 mm. systolic, 80 mm. diastolic; no venous congestion; no œdema; urine normal; Wassermann reaction positive.

Electro-cardiogram.—A normal sino-auricular rhythm with premature contractions, left ventricular in type.

The subjective symptoms gradually improved under treatment, and in the spring of 1924 patient was relieved almost completely of his anginal seizures, an electro-cardiogram at this time (April 2) recording curves characteristic of auricular fibrillation, the murmurs at the base of the heart persisting and a somewhat harsh systolic murmur appearing in the region of the apex impulse.

Dr. F. PARKES WEBER suggested that the onset of the auricular fibrillation as well as the aortic disease itself might be due to the syphilis, which was shown to be present by the positive Wassermann reaction. He (Dr. Weber) believed that cardiac irregularity of the auricular fibrillation type, or an attack of irregularity due to "extra-systoles," might be of service to a syphilitic subject like an attack of angina pectoris might be, if it led to a Wassermann reaction being taken, and thus to the relatively early detection of latent, grave visceral syphilis, that is to say, at a stage when anti-syphilitic treatment could still be of use.¹

A Case of Rheumatic Carditis with Congenital Malformation of the Heart.

By B. T. PARSONS-SMITH, M.D.

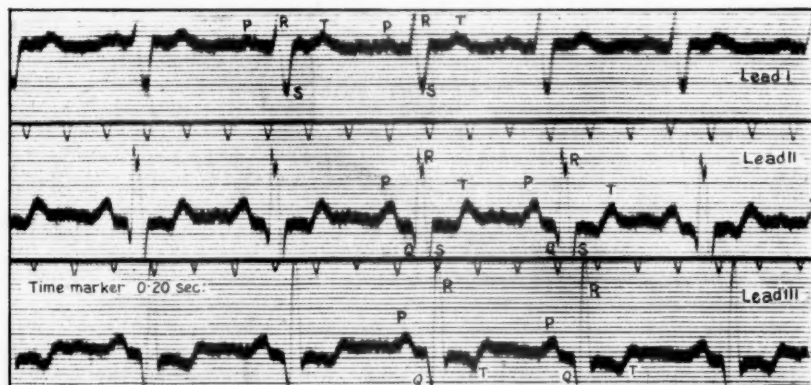
I. G., FEMALE, aged 10. Patient first seen in September, 1925, on account of increasing breathlessness, recurring attacks of bronchitis, and an increasing impairment of exercise tolerance.

Past history.—Bronchitis in infancy; measles and recurring attacks of acute rheumatism; retarded physical development; frequent bronchitis; crises of cyanosis, and inability for sustained effort.

¹ Cf. F. Parkes Weber, "A Case of Auricular Fibrillation and Cardiac Syphilis," *Clinical Journal*, London, 1913, liii, p. 286.

2 Parsons-Smith: *Rheumatic Carditis*; Myers: *Transposition of Viscera*

Physical Examination.—Precordial area, bulging and globular; systolic thrill, maximum in third left space at sternal margin; systolic retraction of apex region well defined in the recumbent position; heart enlarged: area of dullness extends upwards to the second left space and outwards to the apex impulse in the fifth space, $3\frac{1}{2}$ in. from the mid-line; area of dullness fixed and impulse immobile with postural change of the respiratory phases; pleuro-pericardial friction-sounds at base; harsh systolic murmur of maximum intensity in the third left space with upward



conduction to the left infraclavicular region and musical murmur (? pericardial) in same region; pallor of face and tendency to cyanosis of mucous membranes; fingers show early clubbing.

Electro-cardiogram.—Regular rhythm, sino-auricular in type; right ventricular preponderance. R. S. complex broad and notched, suggesting intraventricular block.

Case of Transposition of Viscera.

By BERNARD MYERS, C.M.G., M.D.

H. P., MALE, aged $6\frac{1}{4}$ years. Re-admitted to hospital on July 13, 1925, with congenital morbus cordis, complete transposition of viscera, and congenital talipes equino-varus. The child had had no other complaints. The father and mother are healthy; there are no similar conditions in the other children, and the mother has had no miscarriages. The child is cheerful and bright; mental condition normal. Cheeks, nose, ears, and extremities are of a dark slate colour. The other parts of the body are only slightly cyanosed. Tongue, mouth, lips, and conjunctivæ are of a purple colour. Fingers and toes show very advanced clubbing. Double talipes equino-varus. Legs slightly wasted.

Blood-pressure: systolic 110, diastolic 70. *Heart.*—Apex beat in fifth right interspace. No abnormal pulsations seen. Systolic thrill slight over upper right area of præcordium. The cardiac dullness extends to third right interspace, the fifth right interspace half an inch outside right nipple line and left border of sternum. Systolic murmur—harsh in character and slightly prolonged into the first part of diastole—heard over the whole præcordium. Very marked at pulmonary base and mitral area, where it is conducted out to the right axilla. When previously in

hospital this conduction was not detected. Electro-cardiogram shows inversion of P.R.T. in lead I.

Blood-count.—Hæmoglobin, 147 per cent.; colour index, 0.7; erythrocytes, 9,960,000; leucocytes, 8,600; no abnormal cells seen; Wassermann reaction negative.

In lungs, genito-urinary and nervous systems—nothing abnormal detected. The teeth poor. The stomach, spleen and sigmoid are shown to be on the right side by percussion and X-ray examination; the liver is on the left side (percussion), the cæcum is on the left side (X-ray examination).

This child was shown at the Section for the Study of Disease in Children five years ago.¹ He keeps comparatively well. Recently, several carious teeth were removed under ether and oxygen without the occurrence of any untoward effect.

Case of Congenital Cyanosis.

By BERNARD MYERS, C.M.G., M.D.

D. F., GIRL, aged 5 years 10 months. Admitted to Royal Waterloo Hospital on July 10, 1925, on account of being "backward" mentally, and of "blue colour." The blue coloration was first noticed when she was six months old. It gradually increased to a maximum in about nine months. The child has never spoken and has always been subject to "fits of restlessness." This restlessness has always been most noticeable when she has been frightened in any way, i.e., when taken to hospital.

No history of attacks of extreme cyanosis can be elicited, the only difference in colour being in evidence with changes in the temperature; cold weather slightly increases the cyanosis.

Bronchitis three years ago. No history of any exanthem. Father and mother healthy. One other healthy child aged 3½ years. Mother has not had any miscarriages.

Blood-count.—Hæmoglobin, 165 per cent.; colour index, 0.9; erythrocytes, 9,100,000 per c.mm.; leucocytes, 8,125 per c.mm.; no abnormal cells seen. On spectrum analysis, oxyhæmoglobin is seen to be present.

Nothing abnormal detected in the respiratory, genito-urinary and alimentary systems. Tonsils slightly enlarged.

Complete aphasia. Understands some things which are said. Cranial nerves and fundus oculi normal. Wassermann reaction of cerebro-spinal fluid negative.

The child is restless. Does not sit up very much. Full use of all limbs.

(1) *Head.*—The cheeks, nose, chin, ears, and to a lesser extent the forehead are of a deep purple colour. The cutaneous surface of the rest of the head and neck is of a pale slate colour. (2) *Trunk.*—Pale lilac—more or less uniform. (3) *Extremities.*—Dark red (puce) deepening to purple in the hands and feet. The soles of the feet and palms of the hands are of a dark slate colour. The fingers are markedly clubbed. (4) *Tongue and mouth.*—Dark purple. (5) *Conjunctivæ.*—Dark red.

Blood-pressure.—Systolic 110, diastolic 70. *Heart.*—No thrills or abnormal pulsation detected. Percussion: Area of cardiac dullness. (1) Third left interspace. (2) Fifth left interspace, nipple line. (3) Right border of sternum. Auscultation: No abnormal bruits heard; pulmonary second sound slightly +; tricuspid area, sounds well marked.

Lundsgaard and van Slyke make the following statement²:—

¹ *Proceedings*, 1920-21, xiv (Sect. Study Dis. Child.), p. 4.

² "Cyanosis," *Medical Monographs*, vol. ii.

4 Myers: *Congenital Cyanosis*; Burrell: *Clubbing of Fingers and Toes*

"The blood component responsible for the production of the cyanotic colour is that portion of the hæmoglobin which is not in the state of oxyhæmoglobin, but is either normal, reduced hæmoglobin, or methæmoglobin or sulph-hæmoglobin."

They further refer to the fact that about 5 gr. of reduced hæmoglobin per 100 c.c. of capillary blood appear necessary to cause cyanosis, the amount of oxygenated hæmoglobin also present having relatively little effect. They put it thus:—

"Cyanosis appears to be chiefly dependent on the absolute concentration of the reduced hæmoglobin in the blood rather than on the ratio of reduced to oxygenated."

Among modifying factors they mention—

"thickness of the epidermis, the normal or pathological pigment of the skin; normal and pathological variations in the colour of the blood plasma; variations in the concentration of oxidized hæmoglobin in the blood; variations in number, width and length of blood-filled capillaries in a given surface area; variations in the extent to which the average capillary blood approximates in its unsaturation more nearly to the arterial than to the venous blood, or vice versa." The capillary content of reduced hæmoglobin may be increased by "deficient pulmonary oxygenation, the effect of which is proportional to the total hæmoglobin content, and during passage of the tissues, increased oxygen consumption, the effect of which may be augmented by the presence of an unaerated channel through which venous blood enters the arteries."

Now in cyanosis we think of causes which are due to lung affections such as emphysema and of those due to some error of the heart and blood channels, such as pulmonary stenosis, patent interventricular septum, abnormal position of, or junction between, the great vessels leaving the heart, &c. Erythræmia and enterogenous cyanosis have also to be borne in mind.

In this case the appearance of cyanosis during infancy and its continuous presence since then, with marked clubbing of the fingers and toes; the absence of any enlargement of the spleen; the fairly high colour-index; the absence of any changes on holding up or lowering the hands, also the absence of albuminuria, headache or any apparent dyspnoea, would, I think, be sufficient to negative erythræmia. We can eliminate enterogenous cyanosis because neither methæmoglobinæmia nor sulph-hæmoglobinæmia were found upon investigation.

As there is no lung affection, we can presume that the cause of the cyanosis is not pulmonary, whilst the absence of any heart murmur upon repeated examination allows of the conclusion that pulmonary stenosis, patent interventricular septum (unless the opening be very large), patent ductus arteriosus, &c., are not present. The final choice would appear to lie between a trilocular heart due to a large opening in the ventricular septum, and transposition of the great vessels leaving the heart, or to a junction between the aorta and pulmonary arteries. In a case of an infant dying of congenital cyanosis at the Royal Waterloo Hospital a trilocular heart was found at the necropsy, but the cyanosis was not quite so marked as in this case, and the present patient is nearly six years old. I incline to the opinion that the congenital cyanosis in this instance is due to transposition of the great vessels. So far, no help has been obtained from X-ray examination.

Case of Clubbing of Fingers and Toes.

By L. S. T. BURRELL, M.D.

MALE, aged 40. Quite well until 1905 when he had a hunting accident and broke a rib. A few weeks afterwards he developed clubbing of fingers and toes. The clubbing became very considerable and still persists. There have never been diagnosed, however, any physical signs in the chest either clinically or by the X-ray. His general condition remains quite good and he has neither cough nor expectoration.

The interest of the case lies in the sudden onset of extreme clubbing, which still persists after twenty years without any other signs or symptoms.

Chronic Pulmonary Tuberculosis in a Female aged 36.

By L. S. T. BURRELL, M.D.

THIS patient developed tuberculosis of the lungs eleven years ago, and after a period of sanatorium treatment her general condition improved, although there were extensive signs in the left lung and tubercle bacilli in the sputum. Since then she has gained two stone in weight and is able to lead a normal life without discomfort, except for some dyspnoea. She is always troubled with cough and sputum, and the sputum still contains, and has always contained, tubercle bacilli in large numbers. There are extensive signs of disease in the left lung and some at the right apex. The point of interest in this case is the well-being of the patient after so many years, in spite of the persistence of tubercle bacilli in the sputum.

A Case of Juvenile Acromegaly with Congenital Aortic Stenosis, treated with X-rays.

By E. STOLKIND, M.D.

PATIENT, a girl, aged 19, suffering from general weakness, tiredness, &c.

Family History.—The mother suffers from neurasthenia and headaches. The father, aged 52, has suffered from headaches for about the last twenty years. He is 5 ft. 6 in. high. He has an enlarged nose, slightly enlarged superciliary areas, and specially prognathic lower jaw.

The patient is the youngest of three children. At birth she weighed about eleven pounds. In her infancy the doctors had already diagnosed congenital heart disease. This diagnosis was confirmed soon afterwards by a heart specialist. She began to walk when she was about two years of age. When she was six years old she had scarlet fever, and when aged seven, she had measles. From five to thirteen years of age she suffered from nocturnal enuresis, but after that less often. She left school at the age of fourteen as a "backward girl."

During the past ten years the patient has been growing. The growth was noticed to be particularly striking between 1920 and 1922. Her height is now 169 cm. (5 ft. 6½ in.); three and a half years ago it was 167½ cm.

Her menses began at the age of fifteen; at first every two months, later every month for two days, the amounts being slight in quantity. The liver is enlarged.

Her pulse is about 70, and regular. Brachial blood-pressure - 140/90. The apex beat and heart dullness are about half an inch to the left of the nipple line. There is a systolic thrill in the aortic area; a systolic murmur in the aortic area, less audible at the apex and conducted to the carotid arteries, and in the area of the pulmonary artery. The second sound of the aorta is slightly accentuated. X-ray examination shows that the heart is enlarged to the left, with a rounded apex. The aortic shadow is increased in width, as it often is in cases of aortic stenosis. The diameters of the heart are: transverse 16 cm., longitude 19 cm., transverse diameter of the aorta, 7 cm. There is marked polyphagia. So far, no sugar has been found in the urine. The patient is still very weak, and soon becomes tired after exertion, though not so much as before X-ray treatment. She is shaky and given to stooping; is not so restless as before; is mentally slow, but has lately taken more interest in things than formerly.

X-ray Examination.—(By Dr. J. Douglas Webster): Superciliary areas abnormally developed. Majority of the teeth separated. Lower jaw visibly prognathic. Sella turcica large: posterior clinoid processes exhibit backward-extending processes. Large nasal sinuses, and signs of acromegalic changes in supra-orbital ridge and

6 Stolkind: *Juvenile Acromegaly with Congenital Aortic Stenosis*

mandible. No signs of bony destruction or of deformation. X-ray signs those of early acromegaly.

Ophthalmoscopic Examination.—The eyes were tested by Mr. R. Lindsay Rea and were found to be normal. For the last three and a half years there has been no deterioration in vision. The sella turcica is of the same size as three years ago.

Treatment.—Dr. Douglas Webster has given, dating from November, 1922 to June, 1925, five series of X-ray applications to the pituitary gland. In March, 1925, another series was given. After this treatment the patient's condition improved; she is stronger, brighter, takes more interest in reading, homework, &c., and she talks more. She has grown for the last three and a half years only $1\frac{1}{2}$ cm. (more than half an inch).

Remarks.—In this case after X-ray treatment, improvement of subjective symptoms occurred. As acromegaly is usually subject to spontaneous arrest, it is difficult to say whether the growth has been arrested by the X-ray treatment.

Clinical Section.

President—Dr. G. NEWTON PITT, O.B.E.

A Case of Multiple Bony Lesions for Diagnosis.

By J. H. SHELDON, M.D., M.R.C.P. (Wolverhampton).

PATIENT, a male, aged 20. The family history shows nothing unusual.

He had good health till the beginning of 1916, when at the age of 11, a hard lump appeared on the outside of the right knee. It caused no inconvenience, and was discovered by his mother, quite by chance. He was brought to the General Hospital, Wolverhampton, and the lump was excised. It was considered to be an osteoma, growing from the head of the tibia. At the time of operation, the tendon of the rectus femoris was found to be studded with multiple fibromata. Following this, he returned to school and afterwards worked in a pattern shop. In 1920, he noticed that the lump had returned and was getting bigger, though it caused him no pain. He carried on for two years, and then, as it was preventing him from working he came to hospital again, when a large osteoma was removed from the right knee. He was discharged from hospital again, and almost immediately afterwards growths began to appear in the other limbs. The left knee was the first to be affected, then growths re-appeared on the right knee, and then on the right wrist. The latter began as a soft painless swelling, affecting apparently the whole of the wrist. It was fomented, and eventually burst, discharging thick yellow pus. The wrist has never healed and still discharges a small amount of cheesy material. Similar painless swellings appeared afterwards on the right elbow, on the back of the right arm, and in the right axilla; these also burst and discharged pus—similar, he states, to that of the right wrist. The elbow, arm, and axilla have healed completely. The most recent swelling is that of the right shoulder, beginning in May, 1925, and slowly getting bigger since. The shoulder has been more painful than any of the other joints.

I saw him first on September 30, 1925, when his condition was the following:—

Right Shoulder.—The shoulder is occupied by a large swelling of slightly irregular outline, with three separate eminences pointing anteriorly, laterally and posteriorly, as is shown in the photograph (fig. 1). The swelling is tense, and there is well-marked fluctuation, with reddening of the skin in places. The swelling occupies the axilla, and movement at the shoulder is almost completely lost. The swelling is slowly increasing in size: its circumference in the axillary line being $20\frac{1}{2}$ in. on October 10, 1925, and $22\frac{1}{2}$ in. on November 2, 1925. It was tapped on October 18, 1925, and 10 oz. of thick bile-coloured fluid withdrawn, there being considerable difficulty afterwards in stopping the hæmorrhage; by the next day the swelling had regained its size, and has been slowly increasing since. The fluid withdrawn was sterile, and contained no cells. It showed the absorption-spectrum of urobilin, and gave a positive indirect Van den Bergh reaction, being evidently old altered blood.

Skiagrams (fig. 2) show expansion of the upper third of the humerus, with destruction of bone and loss of the normal outline; yet there is also new formation of bone. There is erosion of the neighbouring part of the outer border of the scapula, with almost complete destruction of the glenoid cavity, and partly of the

coracoid process. There are two circular scars over the middle of the triceps area, where, the patient states, pus was discharged soon after the wrist became affected.

The right elbow is normal. There is $2\frac{1}{2}$ in. of shortening of the right arm.

Right Wrist.—There is an old scar over the posterior aspect of the styloid process



FIG. 1.

of the ulna, which discharges a small amount of caseous material. No growth has been obtained on culture of this, a film showing pus-cells without organisms. Not enough material has been obtained for animal inoculation.

There is destruction of bone with falling-in of the proximal row of the carpus. In addition, there is erosion of bone on the outer side of the distal end of the

ulna, with a profuse growth of exostoses between the radius and ulna, in their lower thirds. There is also an exostosis on the outer side of the radius in its upper half, and an outgrowth of bone of comparatively normal texture from the inner side of the distal end of the radius, growing between the end of the ulna and the cuneiform bone. This outgrowth of bone has formed a new joint with the carpus, displacing the hand radially.

The left arm is normal. Both hips are normal.

Right Knee.—The right knee is partially ankylosed in a quarter-flexed position, with only fifteen degrees of movement. There is a large irregular mass of bone



FIG. 2.—Showing erosion of outer border of scapula and coracoid process, and destruction of the glenoid cavity.

projecting inwards and upwards, growing from the inner side of the head of the tibia, displacing the patella upwards. The patella itself is transformed into a hard, irregular knobby mass of bone. The skiagram (fig. 3), shows also a diffused mass of bone extending into the rectus femoris muscle, from the upper border of the patella.

Right Foot.—There is a hard movable mass of bone of irregular contour lying on the dorsal surface of the ankle-joint, apparently in connexion with the tendons of the extensor digitorum longus. It has a range of movement from side to side of $\frac{1}{2}$ in., and is very slightly movable up and down.

Left Knee.—The anterior surface of the knee-joint is covered by a large mass of hard irregular bone lying below, but continuous with, the patella, and forming a

considerable mass projecting anteriorly. It is practically immovable. A skiagram shows a sharp spur of bone running up into the tendon of the rectus femoris from the upper end of the patella. The space between the lower end of the patella and the tibia is occupied by an irregular mass of bone, growing, apparently, from the tendon of the rectus femoris; this has destroyed a large area of bone on the upper surface of the tibia. The area of destruction is limited by a curved line of thickened bone.

Left Foot.—There is a hard exostosis growing from the inner side of the



FIG. 3.—Showing formation of bone in the infrapatellar tendon, and from the head of the tibia.

navicular bone. The lateral malleolus has lost its normal outline, owing to a diffuse overgrowth of bone.

The dorsal and lumbar spines are normal. The ribs are normal except for an irregular growth of bone from the head of the third left rib. There are exostoses (shown in fig. 4) from the spines of the first two cervical vertebrae.

Numerous changes are present in the skull (see fig. 4). These are: (1) An exostosis springing from the external occipital protuberance. (2) A general thickening of the bones of the vault, in which both tables are concerned. (3) The pituitary

fossa appears to be deepened owing to an overgrowth of both clinoid processes, especially the posterior. (4) There is an irregular outgrowth of bone from the inner table of the frontal bone and the roof of the orbital cavity. (5) There is irregular thickening and new formation of bone on the floor of the skull in the region of the condylar processes.

In connexion with the deepening of the pituitary fossa, it should be noted that the patient's hands and feet are certainly large in proportion to his body. (He takes size eleven in boots.)

The urine is normal, and there has been no albumosuria since he has been under observation: The Wassermann reaction is negative.



FIG. 4.—To illustrate the changes in the skull.

Blood-count, October 13, 1925:—Red cells, 5,200,000 per c.mm.; hæmoglobin, 70 per cent.; white cells, 8,350 per c.mm. Polymorphs, 37 per cent.; lymphocytes, 56 per cent.; monocytes, 8 per cent.; eosinophils, 3 per cent.; basophils, 1 per cent.

The relative lymphocytosis had disappeared by November 2, 1925, when a further count showed:—

Red cells, 5,020,000 per c.mm.; hæmoglobin, 58 per cent.; white cells, 12,350 per c.mm. Polymorphs, 69 per cent.; lymphocytes, 25 per cent.; monocytes, 2 per cent.; eosinophils, 1 per cent.; basophils, 1 per cent.

The temperature is irregular, fluctuating between 99° and 101° F.

I am greatly indebted to Dr. G. E. Dyas and to Miss F. Burke for their help with the skiagrams; to Dr. S. C. Dyke for the pathological investigations, and to Miss L. Garland, the Ward Sister.

Dr. F. PARKES WEBER said he thought that the case was one of multiple osteitis fibrosa, that is to say, Recklinghausen's multiple form of fibro-cystic bone disease. This accounted for the cranial involvement, the pseudo-tumours (sometimes mistaken for sarcomata even after microscopic examination), and the degenerative cysts containing altered blood. The apparent exostoses, however, were a remarkable feature of the present case.

Case of Amyotonia Congenita.

By BERNARD MYERS, C.M.G., M.D.

JOAN B., aged 2, was admitted to the Royal Waterloo Hospital last September. She was unable to walk or sit up properly, but was practically normal mentally.

The condition was first noted when she was 6 months old, but it may have existed from birth. There is no similar case in her family.

On examination she was seen to be normally developed for her age. The muscles of her face and eyes, mastication and deglutition, showed no interference with function. Both legs and arms were limp and the presence of kyphosis was evident in her back when she was made to sit up. The kyphosis disappeared when she was held up by hands placed beneath the axillæ. She was quite unable to support her weight on her legs. The legs could be placed in various unusual positions without difficulty owing to the laxity of her joints, and the dorsum of each foot could be made to just touch the front of the leg without the patient suffering inconvenience or feeling pain. The limbs were well covered, but it was less easy than usual to differentiate the muscles from other soft tissues. The arms and hands were weak, but less so than the lower extremities. When the examiner's hands were placed under the axillæ and moved upwards they were not impeded by the shoulder-muscles in the normal way, but "slipped through" them. The backs of the hands could easily be made nearly to touch the extensor surfaces of the wrists, and the thumbs were freely movable backwards.

She was able to support the weight of her head without difficulty. The knee-jerks were absent; the big toes gave a flexor response; the abdominal reflexes were normal.

A fairly strong faradic current was necessary to produce even a very small response from the affected muscles, and no pain was occasioned or objection made on the part of the child. The response of the facial muscles on the other hand was normal. The response to galvanism was slight and sluggish, but distinctly present. A.C.C. > K.C.C. and A.O.C. > K.O.C.

Examination of the chest and abdomen showed no abnormality. The urine contained no albumin or sugar. The functions of the bladder and bowel were normal. The discs were clearly defined but rather pale. Dr. Bickerton found no macular changes.

The history, the feeding, and the appearances were against the possibility of weakness from rickets; the well-covered limbs and the recent improvement, together with the general picture, negative infantile paralysis; there was no history of diphtheritic paralysis, nor would the course have been similar to that of this case; obstetrical palsy would clearly not account for the picture presented, nor could it be due to the myopathies. Against the diagnosis of the Werdnig-Hoffmann infantile type of progressive muscular atrophy was the age of onset, and the absence of familial or hereditary factors; further, the atrophy did not progress from lower limbs to trunk, neck, shoulders, arms, and hands. In favour of a diagnosis of amyotonia congenita were the appearance of fully developed symptoms either in the first few months of

life or more probably soon after birth, the marked muscular flaccidity, the symmetry, the absence of deep reflexes and of complete paralysis in the affected muscles, no apparent loss of sensibility, the peculiar electrical reactions and the distinct improvement which has taken place generally, although in the arms more particularly, since she came into hospital.

She is receiving massage daily and a few gentle passive movements.

A Case of Aortic Aneurysm (Intrapericardial).

By B. T. PARSONS-SMITH, M.D.

J. M., AGED 69, male.

Past History.—Aneurysm of aorta diagnosed 1894; he was treated in the Heart Hospital by eight months' complete rest in bed, restricted diet, &c., returned to work 1900, and has continued his employment (gardening) until the present time; he now complains of violent attacks of palpitation (paroxysmal tachycardia verified by the electro-cardiogram on one occasion) and occasional indigestion.

Present Physical State. (Cardio-vascular).—Heart enlarged; area of dullness increased to the left, to the region of the apex impulse in the fifth space, $4\frac{1}{2}$ in. from the mid-sternum; percussion dullness in the second right space $1\frac{1}{2}$ in., and in the third right space 2 in. from the mid-line; systolic pulsation and thrill in the third right space; systolic murmur at the apex; heart's action irregular, frequent premature contractions; vessels moderately thickened; blood-pressure 160 mm. systolic, 90 mm. diastolic; no venous congestion; no clubbing of fingers; no objective evidence of raised intrathoracic pressure.

X-ray Examination.—Large, densely opaque, pulsating tumour, with clear-cut margin extending outwards to the right and downwards from the base of the aortic stem in the second and third intercostal spaces; examination in the oblique positions shows that the tumour extends forwards to the chest wall and backwards into the posterior cardiac space, partially obliterating the upper third of the latter cavity; heart enlarged downwards and to the left; margin of left ventricle abnormally convex, and left cardio-phrenic angle poorly defined; diaphragmatic action fair on both sides; lungs appear normal.

Dr. PARSONS-SMITH commented on the length of history—thirty-one years—and was of opinion that the case might reasonably be accepted as cured in so far as the aneurysm was causing no subjective disability at the present time; he further remarked upon the intrapericardial position of the aneurysm, which he felt was largely responsible for the favourable course the case had pursued, the aneurysm having the continuous support of the layers of the pericardium on its outer surface.

Case of Hyperpiesia.

By J. F. HALLS DALLY, M.D.

M. E. F., HOUSEWIFE, aged 62.

Symptoms.—Breathlessness on exertion; occasional substernal pain and oppression; variable slight oedema of ankles within the past two years.

Previous Illnesses.—Measles and tonsillitis as a child. Health otherwise good, except that a right cystic ovary had been removed nine years ago.

Past History.—Has had five children, one of whom died of "tuberculosis." Two miscarriages before birth of last child. *Family History.*—Good.

Clinical Examination.—Height 5 ft. 1 in., weight 10 st. 8 lb. Heart shows left-sided preponderance, apex beat in sixth space $11\frac{1}{2}$ cm. from median line; right border $3\frac{1}{2}$ cm. from median line measured in fourth right space; rhythm regular;

late systolic murmur audible over precordium, of maximum intensity at tricuspid base, conducted to inferior angle of scapula; second sound present. At the aortic base a short rough systolic murmur is conducted upwards to vessels of neck, the second sound being reduplicated.

X-ray Investigation (Dr. J. E. A. Lynham).—Heart shadow of the large transverse sessile type. Aorta broad, but not dilated, of the short, wide type associated with this kind of heart.

Sigma reaction for syphilis is negative in all dilutions.

ARTERIAL PRESSURES.

		Systolic		Diastolic		Differential		Pulse-rate
September 18, 1925	...	320	...	160	...	160	...	108
" 25, 1925	...	320	...	160	...	160	...	108
October 2, 1925	...	310	...	164	...	146	...	88
" 30, 1925	...	310	...	158	...	152	...	88
November 6, 1925	...	295	...	165	...	130	...	90

Comment.—The case is one of interest on account of the unusual height of both systolic and diastolic pressures. Biochemical investigation of the urine shows a normal tidal wave with normal specific gravities, and the ratio of free to combined (ammonia) acid, together with the low total acidity, indicates absence of kidney strain. Albumose is within normal limits, and albumin absent in several specimens examined. There is no evidence biochemically of toxic absorption from the intestines or other source.

A hypersensitive nervous system probably connotes some degree of arterial hypertonicity, the systolic pressure being thereby affected, but it does not explain the high diastolic pressure. Syphilis is a common cause of high arterial pressures, often incapable of reduction, but this cause does not apply here.

I am inclined to regard the case as one of hyperpiesia with characteristic hypertrophy of the heart and changes in the vessels arising independently of renal changes such as occur in the usual forms of Bright's disease. Secondary dilatation of the heart has ensued, with resultant production of a murmur of mitral insufficiency.

Hyperpiesia usually occurs in subjects above middle age, most often between the ages of 50 to 65 years, within which age-limits this patient comes. Its origin is still debatable, but is probably due in part to influences of stress and strain, and in part to absorption of pressor substances as a result of metabolic error, possibly connected with altered liver function. In the present case the ovariectomy may have disturbed the balance of internal secretions in similar wise to the incoördination occurring at and after the climacteric with coincident rise of arterial pressures.

Discussion.—Dr. SAXBY WILLIS asked whether an examination of the fundus oculi had been carried out. In view of the extremely high-blood pressure, it was surprising to find no evidence of renal involvement in the urinary tests carried out, and he thought the condition of the retinal vessels, together with the amount of exudate and hæmorrhage present, was often of great assistance in such cases. He quoted the case of a negro with an advanced renal retinitis, a systolic blood-pressure of 220 mm., and entirely negative urinary findings, who died in uræmic convulsions, and in whom advanced nephritic changes were found post mortem.

Dr. HALLS DALLY, in reply to an inquiry made by Dr. PARKES WEBER, said that he had carefully followed the work of Dr. Geoffrey Evans and others, and was of opinion that certain cases of hyperpiesia could be shown at autopsy to be associated with demonstrable changes in the renal arterioles. Kylin had shown that in similar cases the capillary pressure was normal during life.

In reply to Dr. Saxby Willis, he said that examination of the fundus by Mr. H. Robinson revealed some angio-sclerosis with flattening and fullness of the veins, which here and there were ampulliform where crossed by the arteries. The retina was cloudy, especially around the discs, with slight, very fine opacity of the vitreous in the right eye. The left disc also showed some indistinctness of the edge on the nasal side, where there was slight radial striation. The discs were somewhat hyperæmic. There was no perivasculitis; and there were no hæmorrhages. The fields were full, and the vision good.

Demonstration of a New Sphygmomanometer.

By J. F. HALLS DALLY, M.D.

THIS mercurial manometer, the Baumanometer, of which various models are exhibited, marks an important advance in accuracy in that each instrument is stated by the makers to be individually calibrated by hand against a standard U.S.A. Government mercury manometer. A report from the National Physical Laboratory on my own instrument shows that readings between 40 and 130 mm. Hg are absolutely accurate, whilst above and below these limits an addition of one millimetre only is necessary on a falling pressure. On a rising pressure the readings are accurate up to 150 mm., and above this an addition of one millimetre has to be made except at 160, 270 and 280 mm., which read correctly.

The impossibility of blowing glass tubing of uniform bore makes it requisite to calibrate each rise of the mercury column, which varies with the changing calibre of the glass tube at different levels. The manometer shown is simple and reliable in construction, and can be carried in any position without the mercury falling out. The tube is of large size, and the scale divisions easy to read. In one model the scale can be turned into any vertical position, so that nervous patients are unable to see what pressures are reached. In practice, the Baumanometer has been found very reliable when used with the auditory method of estimation, checked if necessary by the tactile method.

Case of Bronchiectasis: Cerebellar Abscess.

By L. S. T. BURRELL, M.D.

PATIENT, a male, aged 34.

History.—Right pneumonia, 1913. Bronchiectasis developed at right base, but his general condition remained good, and he kept fairly well except for occurrence of cough and expectoration of offensive sputum. In June, 1924, he began to feel giddy and had numbness down the right arm and leg. Right knee-jerk increased and right plantar reflex was extensor. He improved, but still had slight numbness down the right side. In August, 1925, he became worse. Gait unsteady; right leg dragged. Weakness of right arm and leg. Right, plantar reflex extensor; left, flexor. Right ankle clonus. Inco-ordination of right arm. Nystagmus chiefly on lateral movements to right hand; discs normal. Wassermann reaction of blood and cerebro-spinal fluid negative.

Diagnosis.—Cerebellar abscess.

Specimens from a Case of Primary Carcinoma of the Left Bronchus, with Extensive Involvement of the Heart, exhibited by Dr. F. E. Saxby Willis, November 1924.¹

Shown by W. A. YOUNG, M.B.

POST-MORTEM FINDINGS.

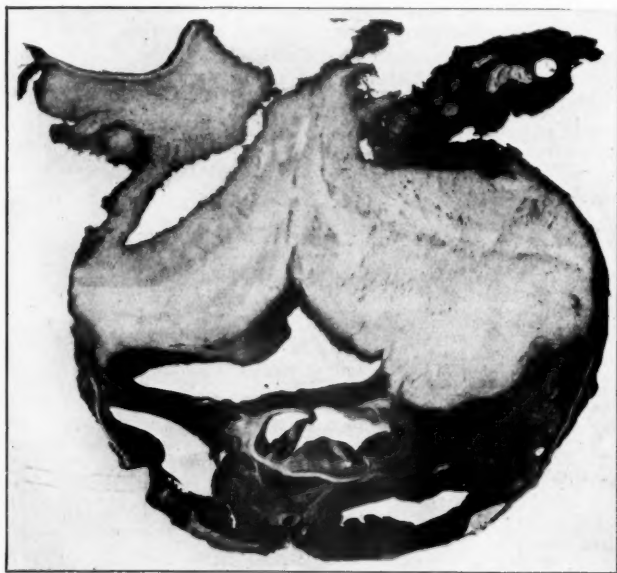
External appearances.—Extreme emaciation; clubbing of finger-nails and toe-nails.

On section.—On the thorax being opened, the heart appeared enlarged to the left. There were dense adhesions on the posterior surface of the left lung. The main tumour mass occupied the posterior and superior mediastina, extended for a short distance into the left lung at the hilum, was attached to the periosteum over the fifth to the ninth vertebral bodies (without erosion of the bone), and had extended along the pulmonary vessels beneath the pericardium, infiltrating the musculature of the

¹ *Proceedings*, 1924-5, xviii (Clin. Sect.), pp. 21, 22.

heart chiefly on the left side to within an inch of the apex. No malignant glands were found in the cervical or supraclavicular groups. A small separate nodule of growth was found on the third left rib, $2\frac{1}{2}$ in. from the costo-transverse joint. This was the only secondary deposit found. The oesophagus was pushed to the left by the tumour, stretched and partly obstructed by it. On opening the trachea the left bronchus was found to be occluded by a fungating tumour half an inch below its orifice. The left lung was small; there was considerable cavitation of its lower lobe, and collapse of the upper lobe. The right lung and glands at the hilum were free from growth.

The heart showed a completely adherent pericardium, fibrosed and thickened down the left margin. A dense mass of tumour tissue had completely replaced the posterior wall of the left auricle and partly of the right auricle, and had extended



Primary carcinoma of left bronchus with infiltration of the pericardium and heart.
(Specimen "B.")

downwards, replacing the upper half of the posterior wall of the left ventricle and the adjacent part of the posterior wall of the right ventricle. In the left auricle and ventricle the tumour tissue had reached the endocardium, but showed no sign of ulcerating through it. Examination of the remaining organs showed nothing of note.

Specimens shown (from the Pathological Museum, Royal Chest Hospital).

Specimen "A." (1) Bronchus partially occluded by growth; (2) growth surrounding descending aorta, &c.

Specimen "B." (1) Growth displacing heart forwards, and extending into musculature of left heart; (2) aortic valves.

Specimen "C." (1) Growth replacing posterior wall of left ventricle, and part of posterior wall of right ventricle; (2) growth reaches endocardium, replacing all muscular tissue but leaves endocardium intact (no ulceration).

Specimen "D." This specimen shows extension of growth on posterior surface of left ventricle towards apex.

MICROSCOPICAL PREPARATIONS.

(1) Carcinoma fungating into left bronchus; growth formed of columns of epithelial cells, outer layers being chiefly columnar, inner cells of transitional shapes; much infiltration of stroma at edge of growth; (2) growth advancing into lung, more diffuse in type; catarrhal changes in surrounding lung; collapse; hyperplasia of bronchiolar epithelium; (3) posterior wall of left ventricle showing muscle displaced by carcinomatous tissue, which reaches a normal endocardium.

ADDITIONAL NOTE BY Dr. F. E. SAXBY WILLIS.

Notwithstanding the gross infiltration of the heart and pericardium, during life no definite physical or X-ray signs of this were present. Precordial pain was a feature, and frequent premature beats were noted. The physical signs were those of an occluded bronchus with massive collapse of the left lung.

Carl Weller has reported 90 cases of primary carcinoma of the bronchus.¹ In only eight of these was there post-mortem evidence of pericardial involvement.

Case of Carcinoma of Bronchus.

By F. E. SAXBY WILLIS, M.D.

W. C., AGED 65, carman, admitted to Royal Chest Hospital on November 3, 1925, complaining of coughing up blood and of pain across the chest.

History.—Cough for two years, very troublesome for last ten months. Sputum first noticed to be blood-stained a year ago, never more than half an ounce of blood coughed up. For the last month streaky hæmoptysis every day. Progressive asthenia and wasting for nine months. Has lost in all two stone in weight. Dyspnoea, now a marked feature, has been increasing for seven months. Appetite has been very poor for three months. Pain across the chest and beneath sternum for three weeks.

Past History.—Influenza in 1918. Pleurisy in 1920 (right-sided pain).

Condition on Admission.—Wasted, cyanosis not very marked. Temperature 101.4° F., pulse 108, respiration 32. Heart: normal in position, no evidence of abnormality. Lungs: on inspection, flattening of left upper chest; restricted movement right lower chest. On palpation, vocal fremitus absent over left upper and right lower chest. On percussion, absolute dullness over left upper chest down to fourth rib and up to the infraclavicular fossa. Resonance impaired in right axilla below fourth rib and below the angle of the right scapula. On auscultation, over left upper chest breath sounds vesicular, but weak. Coarse moist sounds heard over this area when patient was first seen. Voice conduction absent. Over right lower chest the breath sounds are faintly heard, with crepitant râles. At the extreme base breath sounds are absent.

The above physical signs suggest collapsed lung tissue in the areas mentioned, and the fact that the voice sounds are not conducted suggests that the bronchi are occluded. In the left interscapular region, between the fourth and seventh dorsal spines, bronchial breathing is heard.

N.B.—Finger clubbing, though present, is not anything like so marked as in the case shown before the Section in November, 1924, the pathological specimens of which are exhibited to-day.

Paracentesis in mid-axillary line in sixth space revealed no fluid in the right pleural cavity.

Sputum.—No tubercle bacilli. Pus-cells and small mononuclears present.

¹ *Arch. Intern. Med.*, 1913, xi, pp. 314-333.

RADIOSCOPIC EXAMINATION AND REPORT BY DR. KERLEY.

Diaphragm invisible on the right side, moving well on the left side.

Right Lung.—The lower zone is opaque, the opacity diminishing towards the periphery. There is undoubted consolidation and thickened pleura here (? effusion). The picture closely resembles that of bronchiectasis.



Carcinoma of bronchus, October 25, 1925.

Left Lung.—The hilum is enlarged to about five times its normal size, like an inverted bowl in shape, and from it dense wavy striations run into the parenchyma of the lung, the so-called "woolly infiltration." The picture is almost a classical one of bronchial carcinoma.

A further X-ray photograph taken a fortnight later showed extension of the shadow in the lower zone of the right lung and suggests that this is due to an extension of new growth.

Case of Polycythæmia Rubra Vera (Vaquez Disease) treated twice with application of X-rays to the Bones ; Duration of Improvement.

By E. STOLKIND, M.D.

PATIENT, a male, aged 53, complained of giddiness, general weakness, pains in the legs, &c. During the last five years he has often had hæmoptysis. In 1921 there were all the signs of polycythæmia vera; the same are also present in a less degree now, i.e., cyanosis of the face, nose, lips, mouth, cyanotic clubbed fingers, "polished" nails, injected conjunctivæ, enlarged and palpable spleen and liver, &c. Wassermann blood-test repeatedly negative. Brachial blood-pressure 140 to 150 (systolic) and 90 (diastolic). Red blood-cells, 9,500,000 to 10,000,000; hæmoglobin, 150 per cent.; colour index, 0'8; white cells, 16,400. (For particulars see the account I have given in the *Proceedings* of this Section [10].) As a treatment a doctor advised the extraction of all his teeth; this advice was followed without good result. Venesections, as well as the administration of benzol (3 to 6 c.c. per diem for seven weeks) were without any result. Very slight improvement followed after a rest cure and after administration of potassium iodide. A considerable subjective improvement followed only after eleven full applications of intensive X-rays to the sternum, thighs, legs and arms. After the X-ray applications the red cells were found to number 7,000,000.

The improvement lasted for about ten months, and then again the patient gradually became worse. He suffered from pressure in the head and from headaches; later from frequent attacks of severe pain in the big toes, which often became black-blue and swollen under and near the nails, it seemed like some transitory form between Raynaud's disease and erythromelalgia; the pain lasted sometimes for many days. He often had pain in the legs. About one and a half years after X-ray treatment he again suffered from his worst symptoms: tiredness, giddiness, &c. The repeated blood-counts showed a gradual increase of the number of red cells. For instance, September, 1924:—

Red cells, 9,350,000; hæmoglobin, 134 per cent.

White cells, 13,800.

Colour index, 0'72.

The differential count of white cells yielded:—

Polymorphonuclear neutrophils, 84 per cent.; intermediary myelocytes, 1 per cent.; eosinophils, 1'5 per cent.; leucocytes: small, 12'5 per cent.; large, 0'5 per cent.; mast cells, 0'5 per cent.

Blood-count in July, 1925:—

Red cells, 9,860,000; hæmoglobin, 136 per cent.; colour index, 0'69. White cells, 22,400. Differential leucocyte count: polymorphonuclears, 87 per cent.; lymphocytes: small, 7 per cent.; large, 2'5 per cent.; large mononuclears, 0'5 per cent.; eosinophils, 2'5 per cent.; mast cells, 0'5 per cent.

The blood was distinctly viscid, requiring a decided effort to suck it up into the red pipette and spreading on the slides with difficulty in a thin film. Colour, dark bluish-red. The red cells showed moderate anisocytosis. Leucocytes showed a distinct increase, especially the polymorphonuclears, which were of distinctly larger size than normally, i.e., a high number of lobes. The platelets were also very numerous and large.

Between July 28, 1925, and September 24, Dr. J. H. Douglas Webster gave seven full applications of intensive X-rays (50 to 75 per cent.) to the thighs, legs and arms.

Again a considerable improvement of the subjective symptoms followed. There occurred a slight X-ray erythema in the thighs and legs.

Blood-count, October 6, 1925:—

Red cells, 9,784,000; hæmoglobin, 126 per cent.; colour index, 0'6.

White cells, 10,400: polymorphonuclears, 78 per cent.; lymphocytes, 10'7 per cent.; large mononuclears, 2'6 per cent.; eosinophils, 3'5 per cent.; mast cells, 0'9 per cent.

Blood-count, October 30, 1925:—

Red cells, 8,420,000; hæmoglobin, 136 per cent.; colour index, 0'81.

White cells, 10,400; polymorphonuclears, 81 per cent.; lymphocytes: small, 11 per cent.; large, 2'5 per cent.; large mononuclears, 0'5 per cent.; eosinophils, 4 per cent.; mast cells, 1 per cent.

Blood, dark and viscid. Distinct anisocytosis. Red corpuscles crowded into a "mosaic," even where very thinly spread. Leucocytes, polymorphonuclears, distinctly large and multilobed; 4, 5 or even 6 and more. Platelets, numerous and considerably larger than usual. I have to thank Dr. Carnegie Dickson for undertaking the blood examination.

REMARKS.

The X-ray treatment has so far produced only a temporary improvement in the subjective condition. The number of red cells and the percentage of hæmoglobin are reduced also only temporarily. The improvement may last from a few months to one year or two years, or even more.

There are on record only a few cases of erythræmia (Vaquez) that have been treated with application of X-rays to the bones and observed afterwards for more than a year. These are the cases reported by Guggenheimer [1], Johnson [2], Kaufmann [3], Luedin [4], Mosenthal [5], Pendigrass [6] (X-ray treatment of the bone-marrow was begun in 1907, continued during 1909 and carried on until March, 1910). Also the cases of Rydgaard [7], Schoening [8], Steiger [9], Verity [11] and a few others. In many of these cases the result was the same as in my case.

REFERENCES.

- [1] GUGGENHEIMER, *Zeitschr. f. ges. physik. Ther.*, 1923, xxvii, p. 87. [2] JOHNSON, *Journ. Amer. Med. Assoc.*, 1925, lxxxiv, p. 1253. [3] KAUFMANN, *Klin. Wochenschr.*, 1923, ii, p. 770. [4] LUEDIN, *Strahlenther.*, 1920, x, p. 213. [5] MOSENTHAL, *Med. Klin.*, 1923, xix, p. 1158. [6] PENDIGRASS, *Amer. Journ. Med. Sci.*, 1921, cxliii, p. 723. [7] RYDGAARD, *Acta Radiol.*, 1923, xi, p. 243. [8] SCHOENING, *Klin. Wochenschr.*, 1922, i, p. 172. [9] STEIGER, *Schweiz. med. Wochenschr.*, 1923, liii, p. 376. [10] STOLKIND, *Proc. Roy. Soc. Med.*, 1923, xvi (Clin. Sect.), p. 35. [11] VERITY, *Med. Journ. & Record*, 1924, cxx, p. 319.

Case of Hypopituitarism in a Boy, with Epilepsy; Sella Turcica reduced in Size.

By E. STOLKIND, M.D.

PATIENT, a boy, aged 16, is suffering from epileptiform fits, mostly nocturnal, general weakness, occasional vomiting, &c.

Father was a soldier who died from aortic aneurysm, in all probability syphilitic, at the age of 34. Mother and the younger sister healthy.

The boy was regarded as normal until the end of his fourth year, when there occurred a series of convulsive seizures which gradually became more severe and frequent. When 5 years old the patient began to attend school, where the doctor diagnosed "heart disease." When between 8 and 9 years of age he was obliged to leave the school owing to the fits occurring during his lessons.

The attacks occur almost every day, mostly at night time, two to eight and sometimes more; they last for from one to ten minutes. In the daytime the attacks are usually preceded by an aura—"some feeling in the eyes and face"; always with loss of consciousness and incontinence of urine. During the fits observed in the West End Hospital for Nervous Diseases, the patient called out, then he became rigid; clonic and sometimes tonic movements of all the body followed; he was very cyanosed, with his pupils dilated, and eyes turned to the right, &c. There are periods of polyphagia, polyuria and polydipsia—"he is always thirsty and could drink all the time."

He is a pale, obese boy, 5 ft. 1 in. high. Panniculus is especially abundant over the pectorales, abdomen and hips: rather a feminine type of distribution. His weight varies according to the epileptic attacks: when these are frequent, he becomes thinner; when they are "minor," or only one or two daily, he gains in weight. For instance, in July, 1924, after the "good" period, his weight was 9 st. 10 lb.; in February, 1925, after a "bad" period, only 8 st. 7 lb. He is always stooping and shaky. There is often dribbling of saliva. He is very weak and unable to get up during his "bad" period, walks with difficulty or is even unable to walk. "He is then like a baby." He can walk more or less freely during his "good" periods. During the "bad" periods he is more or less stuporous, very dull, unclean in his habits, e.g., passes urine or stools on the floor or in bed. He is mostly dull, very irritable, obstinate, with lack of self-control. He is backward, but answers simple questions intelligently. Bilateral weakness of the face, spastic convergence. Eyes, normal. Brachial blood-pressure 70 (diastolic) and 110 (systolic). Sometimes there are extra-systoles. Heart normal. Sella turcica reduced in size and with clinoid processes overlapping. After administration of 200 grm. of glucose, no sugar in the urine; after 300 grm. slight glycosuria appeared in the first hour, no sugar in the second hour. The resting blood-sugar is 0.13 per cent. The blood-sugar curve—following the oral administration of 50 grm. of glucose—is, after one hour, 0.168; after one and a half hours, 0.162; after two hours, 0.106. Thus the blood-sugar curve is normal.

Wassermann blood-test negative.

The patient was under treatment in other hospitals without any results. He has been under my treatment for about two and a half years. I have tried pituitary whole gland, as well as pituitary posterior, $7\frac{1}{2}$ gr. daily together with luminal $2\frac{1}{2}$ gr. twice daily and sodium bromide 30 to 50 gr. daily, without any result. I am now trying to increase the doses of pituitary gland and to add also thyroid, and I am giving injections of posterior pituitary gland, but so far without any effect.

REMARKS.

The important points are the high sugar tolerance; the periods of polyphagia, polydipsia and polyuria, of adiposity—increased or diminished according to the frequency and gravity of the epileptic fits; the apathy, drowsiness, weakness, mental dullness, &c., especially during the "bad" periods, which are, in my opinion, the result of deficient secretion from the diminished pituitary gland, especially the posterior lobe. He is not an imbecile.

It is a question whether the epileptic fits, &c., can be relieved by sellar decompression, i.e., by resection of the overlapping clinoid processes.

October 9, 1925

Cases of Bronchiectasis.

By DOUGLAS FIRTH, M.D.

Dr. DOUGLAS FIRTH showed two cases of bronchiectasis, with X-ray negatives, taken after the injection of lipiodol into the bronchi.

The technique of lipiodol injection was described by Dr. Burrell.



Clinical Section.¹

President—Dr. G. NEWTON PITT, O.B.E.

Professor H. MACLEAN, M.D., gave a demonstration on the "Methods of Determining Renal Efficiency."

Cases Illustrating the Effects of Glandular Treatment.

By H. GARDINER-HILL, M.B.

(1) CASE OF DEFECTIVE GROWTH AND MALNUTRITION TREATED BY ANTERIOR LOBE PITUITARY EXTRACT.

C. C., aged 12. This boy's height when treatment was begun was 118 cm., the average for a boy of his age being 140 cm. His weight was 3 st. 10 lb., as against the average for age of 5 st. 6 lb. Development was below average; mentality alert. Bone development was delayed. Sella turcica was about normal. Wassermann reaction negative. Sugar tolerance was decreased. Illustrations of the curve before and after treatment are shown with the patient.

He has been treated with anterior lobe pituitary extract since November, 1924, the dose being gradually increased to 15 gr. a day of the desiccated extract.

In the course of a year he has grown 6 cm., a rate which is slightly in excess of the average for age. During the previous ten months under observation he only grew 3 cm. Bone development has advanced. Weight has increased to 4 st. 7 lb., a gain of 8 lb. in the year. During the previous year he only gained 2 lb.

This case illustrates the effect of anterior lobe pituitary extract on growth and carbohydrate metabolism.

(2) CASE OF INFANTILISM WITH DEFECTIVE GROWTH TREATED BY ANTERIOR LOBE PITUITARY EXTRACT.

F. V., aged 12. This boy was sent to hospital on account of lack of growth which was first noticed at the age of 8. Between the years of 8 and 11 he grew at the rate of 1 inch per annum. During the following year (11-12) he grew $\frac{1}{2}$ inch (1'25 cm.). This is considerably below the average rate of about 5 cm. per annum for a boy of his age. He has always been remarkably free from illness.

When first seen his height was 106 cm. (average for age 140 cm.). Symphysis-vertex measurement, 54'5 cm.; symphysis-soles, 50'5 cm. Sella turcica about average size. Visual fields normal. Bone development corresponded with that of a child of 7, being considerably delayed (X-rays shown with the patient). The centre for the semilunar bone of the wrist should normally appear at the age of 5; his is only just appearing in the right wrist and has not appeared in the left.

On anterior lobe pituitary extract he has grown 7'25 cm. in the year, as against 1'25 in the previous year. The X-ray photographs show the advance in bone development. There are now well-marked centres for the semilunar bones in each wrist; the centre for the pisiform, which normally should appear at the age of 12, is also present.

During the year he has gained 7 $\frac{1}{2}$ lb. in weight, and his carbohydrate metabolism has improved to a corresponding extent. A previously decreased tolerance is now normal.

This case illustrates the effect of anterior lobe pituitary extract on growth, carbohydrate metabolism and bone development.

¹ Meeting held at St. Thomas's Hospital, December 11, 1925.

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(3) CASE OF INFANTILISM WITH PRIMARY AMENORRHOEA TREATED BY ANTERIOR LOBE PITUITARY EXTRACT.

D. H., aged 19. This girl was sent for examination because menstruation had not begun. Pelvic examination in the Gynaecological Department showed that the uterus was of the infantile type and extremely small. Height was only 146 cm.; weight, 5 st. 8 lb. She is said not to have grown since the age of 10. Bone development delayed, the epiphyses being wide apart. Her mentality is infantile.

In addition to her menstrual trouble she also suffered from periodic frontal headaches, which were accompanied by epistaxis. Her carbohydrate tolerance was considerably decreased.

She has been treated with anterior lobe pituitary extract for five months. She has grown 2.5 cm. in that time, that is, at the rate of 5.5 cm. per annum. Her menstruation has not begun, but her periodic headaches, with epistaxis, have entirely ceased. Her weight has remained stationary. Her sugar tolerance is now increased.

The result illustrates the effect of anterior lobe pituitary extract on the metabolism of this type of case, but this extract does not seem to be effective in inducing menstruation in cases of primary amenorrhœa.

(4) CRETIN TREATED WITH THYROID EXTRACT.

F. H., aged 31. This patient received thyroid treatment for two years at the age of 14, and for six weeks at the age of 21. She is the eldest of four children. She has always been very diminutive for her age. Her height when she came to hospital a year ago was 125 cm. Her weight was 5 st. Menstruation began at the age of 21 and has always been regular; rhythm 4/28. Bone development has been delayed. X-ray shows the epiphyseal line at the lower end of the radius and ulna. Her sella is rather large for a person of her size.

Her sugar tolerance when she first came under treatment was extremely decreased. The curves are shown with the patient.

This patient has been treated with gradually increasing doses of thyroid extract (desicc., Armour's). She is growing at the rate of nearly 2 cm. per annum at the age of 31. Her present carbohydrate tolerance curve is normal. Her general condition has improved considerably. When she first came to hospital she was invariably cyanosed and lethargic. At the present moment there is very considerable difference in both these respects.

This case is shown to illustrate the characteristic effect of thyroid extract on the metabolism of an untreated cretin.

(5) CRETIN.

M. G., aged 9½. This child was treated with thyroid extract from the age of 3 until November, 1924. Treatment was then discontinued for ten months; during that time the patient increased in weight by 2 st.

When she was seen two months ago her sugar tolerance was considerably increased. Weight was 5 st. 9 lb. Bone development well up to the average. Her sella turcica was above the average in size for a child of her size.

She has been treated for the last two months with thyroid extract up to 3 gr. a day. She has lost 11 lb. in weight in this time. Her last sugar tolerance curve, done a week ago, was considerably nearer the normal than the previous one. Her mentality has markedly improved.

This case is shown to illustrate (1) normal bone development in a treated cretin; (2) the rapidity with which these children relapse when treatment is left off; (3) the rapidity with which their subthyroidic symptoms clear up when treatment is resumed.

(6) CASE OF INFANTILISM TREATED BY THYROID AND ANTERIOR LOBE PITUITARY EXTRACTS SIMULTANEOUSLY.

W. H., aged 15. This boy was brought to hospital for wasting. He had been losing weight for eleven months. His mother said that he was always extremely sleepy. When first seen he appeared to be subthyroidic; his mentality was very slow; his circulation bad and his general appearance puffy.

Carbohydrate tolerance was considerably decreased. Bone development about normal. Sella turcica slightly below the average in size. Height was 135 cm., the average for a boy

of his age being 160 cm. He was considerably undergrown. Weight was 4 st. 5 lb., as against the average of 7 st. 7 lb.

He has been treated on gradually increasing doses of thyroid extract (desicc.) and anterior lobe pituitary extract (desicc.).

His subthyroidic symptoms have very much decreased. His rate of growth has been considerably increased; he has grown 8 cm. in ten months, which is at the rate of 9.6 cm. a year. His weight has increased to 5 st. 4 lb., a gain of 13 lb. in ten months. This improvement in general condition is associated with improvement in carbohydrate metabolism. The curves before and after treatment are shown with the patient.

This case illustrates the beneficial effect of administering thyroid extract and anterior lobe pituitary extract simultaneously. The tolerance to thyroid seems to be increased.

(7) ADOLESCENT OBESITY ; PITUITARY TYPE. TREATED BY THYROID EXTRACT.

I. B., aged 13. This girl has recently been brought to hospital for obesity. Her weight is now 13 st. 9 lb. She is overgrown for her age, her height being 155 cm. Her obesity developed after diphtheria at the age of 8. Previous to that she was not abnormally stout. Menstruation commenced at the age of 12, but the periods are irregular and come on at intervals of about three months only. She eats more than the average child. Her carbohydrate tolerance is considerably increased. (Curve shown.)

Bone development advanced, the epiphyses of the hands and wrists having all united at this early age. Her sella turcica was reported on as below the average size.

She has only recently commenced to undergo treatment with thyroid extract.

The case is shown to illustrate the type of so-called pituitary obesity in which the latter develops in association with a period of accelerated growth—the bone development is correspondingly advanced. Menstruation in these patients, after beginning early, usually becomes more and more irregular and defective. Treatment with thyroid and whole gland pituitary extracts often exerts a beneficial effect in reducing obesity and improving the metabolism and menstruation.

(8) CASE OF METRORRHAGIA TREATED WITH EXTRACT OF CORPUS LUTEUM.

R. F., aged 15. This child was sent to hospital for metrorrhagia. Her periods began at the age of 11½ and have always been irregular, occasionally lasting for months at a time. On the present occasion the menstrual losses have continued for ten months without intermission.

She is a well-developed girl of average height, slightly below average weight. Bone development is considerably advanced. The epiphyses of her hands and wrists have all completely fused. This should normally occur at the age of 18 to 20. The epiphyses of the radius and ulna normally fuse at about the age of 23 to 25. Pelvic examination shows the uterus to be normal in size.

This case is shown to illustrate a point which is often found in these cases of puberty metrorrhagia: advanced bone development in association with physical characteristics which are rather above the average.

She has been treated with extract of corpus luteum, 5 gr. t.d.s. for six weeks. This appears to have exerted a beneficial effect. Menstruation had, previous to treatment, been continuous for ten months. Since treatment the losses have stopped with a fourteen days' clear interval.

Case of Eunuchoid Type with Undescended Testicles.

By H. GARDINER HILL, M.B.

J. S., AGED 13. This child was brought to hospital for backwardness. His general development was also below the average. Previous to a year ago both testicles had been undescended.

He is tall and above the average height for his age; height 155 cm., against the average for age of 144 cm. He is rather below the average weight for a boy of this height, his weight being 6 st. 1 lb., as against 6 st. 11 lb. He is considerably longer in the limb than he is in the trunk; his symphysis-vertex measurement is 69 cm.; symphysis-soles 86 cm.

Sugar tolerance somewhat decreased. Bone development is well up to the average. Epiphyses widely open. Sella turcica below the average size.

He is shown to illustrate a mild degree of eunuchoid bodily configuration, which is so frequently seen in backward children of this type with undescended testicles.

So far no glandular treatment has been undertaken.

[January 8, 1926.]

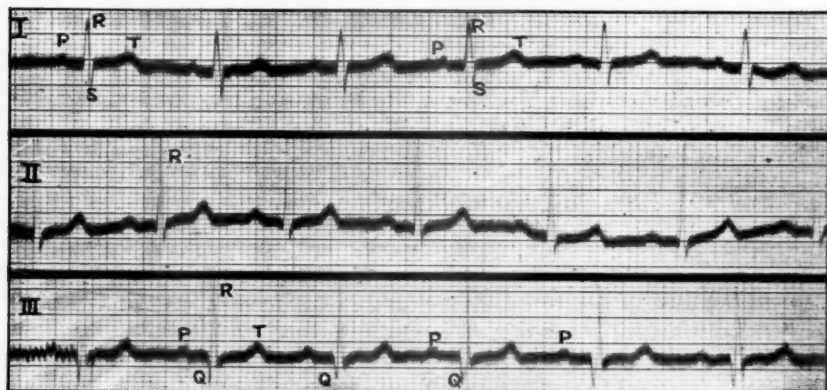
A Case of Patent Ductus Arteriosus.

By DOUGLAS FIRTH, M.D.

PATIENT, L. T., a girl, aged 14½, who was quite well up to the age of 7 years. She then had rheumatic fever, for which she was kept in bed for seven months. Since that time she has had slight dyspnoea, and occasional pains below the apex of the heart. She was admitted into hospital in November last for sore throat, pains in the limbs and some pyrexia, which subsided rapidly under salicylates.

There is no cyanosis nor clubbing of the fingers. The apex beat of the heart is in the fifth space, 3¼ in. from the mid-sternal line, and the area of cardiac dullness extends to the sternal edge on the right and to the third rib above.

A faint thrill, late systolic and diastolic in time, can be felt in the second left



interspace, 2 in. from the mid-sternal line. At this spot, a swishing double murmur is heard, also late systolic and diastolic, in the midst of which a sharp second sound is audible. This murmur is conducted towards the left shoulder. At the apex a soft systolic murmur, conducted outwards towards the axilla, is heard.

Although the girl has had one severe attack of rheumatic fever, and at least one other slight one, the signs at the base of the heart do not seem to be compatible with an acquired lesion. On the other hand they closely resemble the signs given by Gibson as those of patent ductus arteriosus. It is true the thrill is feeble and the shock of the closing of the semi-lunar cusps cannot be felt, but I would venture to suggest that these modifications are due to the acquired lesion.

The electro-cardiographic report by Dr. C. B. Levick states :—

There is, perhaps, slight preponderance of the right ventricle, but I consider that the curves rest within the limits of normality.

The P summit is broad and flat, as often occurs in mitral stenosis, but the curves in general are of the type commonly occurring in cases of patent ductus arteriosus.

Functional Dysphagia in a Girl.

By BERNARD MYERS, C.M.G., M.D.

G. E., AGED 13, was admitted to the Royal Waterloo Hospital two years ago on account of slight enlargement of the thyroid and dysphagia. The thyroid gland did not seem to be the cause of the dysphagia, and this opinion was upheld by a surgical colleague, and also by Sir James Berry, who kindly came down to see the case. The X-ray examination showed no difficulty in swallowing or any defect.

However, she reiterated her difficulty in swallowing, and one day declared that she was quite unable to swallow anything. Persuasion was useless, but the sight of a stomach tube caused her to discover that she could swallow fluids; after this, when told that she could and must swallow solids she was able to do so.

She described her symptom as a contracting feeling which appeared at the back of the throat on the thought of swallowing food.

She is a well-developed girl and quite healthy, but distinctly neurotic. There are five children in the family and two more are also neurotic.

The patient had complained of frontal headache. She had dark rings around her eyes. The merest trifles excited her, and she seemed incapable of exercising self-control. At times she stated that she could not breathe properly. She had suffered from night terrors, and when the possibility was suggested to her she came to the conclusion that she had no strength in her legs; she worried absurdly over school work and "got on the nerves" of her brothers and sisters unduly. There was a startled look in her eyes, and it only needed a little suggestion for her to become hysterical.

It would almost seem as if the imaginary difficulty in swallowing was of the nature of a habit spasm, as she was imbued with the idea that the slightly enlarged thyroid would not allow her to swallow. She has improved greatly after taking bromides, valerian and after undergoing treatment by suggestion.

Postscript, March 22, 1926.—I saw her to-day and found that she had not experienced any difficulty in swallowing liquids or solids for over two months. She enjoys excellent health and has grown a good deal taller.

Ascitic Tuberculous Peritonitis with Large Masses.

By BERNARD MYERS, C.M.G., M.D.

R. A., AGED 11, was admitted to the Royal Waterloo Hospital during 1924, for generalized enlargement of the abdomen. She was taken suddenly ill a few days before admission, and her abdomen had rapidly become swollen.

She looked distinctly ill, a hectic flush was present, her temperature was 103° 5' F. and her abdomen was markedly enlarged and contained much fluid. Some 10 c.c. of the fluid was withdrawn for injection into a guinea-pig, but unfortunately through some error in the laboratory it was not injected. The temperature was raised for six weeks, usually reaching about 101° F. daily but occasionally 103° F. There was a slight affection of the right apex, but no activity was discovered. She was so desperately ill for the first fortnight that her recovery was not expected; however, after that period the fluid began to be absorbed, and in two to three days had apparently all disappeared, as none could be elicited, or obtained by a needle. Very large masses were now palpable in the abdomen, one just above the umbilicus being the size of a grape-fruit, while another enormous mass was lying transversely across the upper part of the abdomen. Four or five nodular masses the size of tangerines were apparently attached to the parietal peritoneum. Personally, I can state that I

28 Myers: *Ascitic Tuberculous Peritonitis*; Burrell: *Chronic Œdema*

had never seen previously such large masses in tuberculous peritonitis. They were slowly absorbed, although the process took about twelve months.

At the present time no masses or lumps can be felt in the abdomen, although there is a distinct suggestion of adhesions in the region above the umbilicus. The bowels act daily, however, and there is no vomiting, nor flatulence, nor colic. The appetite is excellent. She sleeps well and feels and looks in perfect health. The temperature has been normal for some months and she has put on a large amount of weight and grown considerably.

In treatment, rest in bed, iodine, de-fatted tuberculin, malt and ol. morrhue, were employed and then she was sent to a convalescent home for six months and she received appropriate feeding. I have no reason to believe that the alipoid tubercle bacillary emulsion played any part in her recovery. Nature is the best healer in these cases and we merely endeavour to give her every help to do her work.

This patient is only shown as an instance of the disappearance of such large tuberculous masses from the peritoneal cavity with complete restoration of health.

Case of Unusual Chronic Œdema.

By L. S. T. BURRELL, M.D.

MRS. F., aged 26.

Seven years ago there appeared a sudden swelling of the left instep and then of the ankle, and then half way up the leg. This swelling varies in size but has never disappeared. It has never been painful.

A month ago a similar swelling of the right instep set in. This comes and goes and is very slight now.

Once, about three years ago, she had a sudden swelling on back of left hand and this lasted about two weeks and has never returned.

Dr. F. PARKES WEBER said he regarded Dr. Burrell's case as one of acquired (apparently non-familial) "trophœdema" of the left leg. A similar condition was beginning to show itself in the right foot. The swelling in the left lower extremity had probably not really commenced suddenly; the patient one day (after standing) noticed that the dorsum of her left foot was swollen, and since then the swelling had gradually extended above the ankle. The œdema might be intermittent at first. Although doubtless the swelling could at present be temporarily completely got rid of by rest in bed and bandaging, it would probably ultimately lead to a minor form of "elephantiasis nostras" of both legs. Cases of the kind in young women were not exceedingly rare, one or both legs being affected.¹ The temporary swelling in the hand was doubtless of another nature.

Demonstration of Cases.²

By H. BATTY SHAW, M.D.

(I) CASE OF A CHILD SUFFERING FROM DOUBLE MITRAL DISEASE.

Gradually and without any manifestations of pain or shortness of breath a condition was developed in which the breath sounds of the left lung were lost, the left chest remaining resonant to percussion: it was presumed that this condition was due to the occurrence of a slowly developing spontaneous pneumothorax, as the manometric readings of the intrapleural pressure were similar to those met with in artificial pneumothorax.

¹ Compare F. Parkes Weber, "So-called Trophœdema of the Left Lower Extremity," *Proc. Roy. Soc. Med.*, 1908, ii (Clin. Sect.), p. 52; Weber, *Trans. Med. Soc. Lond.*, 1912, xxxv, p. 370 (a young woman, with chronic œdema of the right leg, of the same nature). The familial cases of the same nature were first described by M. Nonne (1891) and W. F. Milroy (1892).

² Meeting held at the Hospital for Consumption and Diseases of the Chest, Brompton, February 12, 1926.

(II) CASE OF PERSISTENT DULLNESS AND WEAK BREATH SOUNDS WITHOUT THE PRESENCE OF RÂLES IN A YOUNG CHILD.

This child was ill with cough and severe fever of four weeks' duration a year ago. Ever since this illness the above signs had been present. Radiographically it was shown that the dullness was of uniform character, with the exception of a few doubtful areas of infiltration. The case was one possibly of confluent tuberculous pneumonia, but the nature of the infection cannot be established by bacteriological examination as there is no sputum and the stools show no tubercle bacilli.

(III) A PATIENT, AGED 73 YEARS, WHO HAD BEEN CONTINUOUSLY TREATED AT THE BROMPTON HOSPITAL FOR FORTY YEARS FOR COUGH, SHORTNESS OF BREATH, AND EXPECTORATION.

She revealed signs of excavation and fibrosis of the right lung. The presence of tubercle bacilli had been established only once, thirty-four years ago, and they were numerous. Many examinations made before and since that date revealed no tubercle bacilli. Evidently for many years she had been a case of consumption, which was quite independent of the influence of a tuberculous infection. Radiography revealed the presence of numerous calcified areas present in the lungs which obviously were sealed up so firmly as to allow of no liberation of their contents during the last thirty-four years.

(IV) CASE OF A WOMAN, AGED 40, KNOWN TO HAVE HAD HEMOPTYSIS, COUGH, EXPECTORATION, WASTING, SWEATING, AND WHO REVEALED SIGNS OF CATARRH AT THE RIGHT APEX DURING THE PREVIOUS THREE YEARS.

Her sputum is and always has been free from tubercle bacilli, and radiograms failed to establish the presence of any shadows suggesting tuberculous infiltration of the lung. This patient has had a cough every winter since childhood, but ever since 1917 it has been much more severe and expectoration has been abundant.

Demonstration of Radiograms, Museum Specimens and Drawings of Microscopic Sections of Lungs representing the changes met with in so-called "Pulmonary Tuberculosis."

By H. BATTY SHAW, M.D.

It was clear that the conception that all cases of debility, anorexia, wasting-fever, night sweats, &c., associated with cough and expectoration,—may be of mucus, of pus or of blood,—and the existence or not of signs of pulmonary disease such as apical catarrh, consolidation and excavation, should be considered, *ipso facto*, to be cases of "pulmonary tuberculosis," whether or not tubercle bacilli were present in the sputum, was unjustifiable. All these signs and symptoms could be produced by the action of catarrho-pyogenic organisms without the assistance of tubercle bacilli: indeed the latter organism unaided by catarrho-pyogenic organisms could only produce changes in the lungs which were beyond the reach of the clinician, unless he was helped by the radiographer. Despite the cautious attitude of radiographers of experience, it was, however, far too common to read the confident reports of radiographers that a patient was suffering from "pulmonary tuberculosis" owing to the presence of so-called "areas of infiltration" or "woolly patches" in a radiogram. Microscopic examination of these small areas showed that though many of them were tuberculomata, others were due to small abscess- and broncho-pneumonic-formations around the smaller bronchioles.

So far from catarrho-pyogenic infections being mere terminal episodes in cases of "pulmonary tuberculosis," they were responsible for the liberation into the blood-stream of tubercle bacilli, previously safely locked up in old tuberculous deposits, and

so led to that development of miliary tuberculosis of the lungs which presented the features of vascular dissemination. Moreover the evidence that tubercle bacilli could produce the pneumonic consolidation met with in cases of "pulmonary tuberculosis" was based on the slenderest of very debateable evidence: it was impossible for tubercle bacilli to invade vessels and cause hæmoptysis, for they caused first occlusion and then absorption of blood-vessels; lastly, cavities could be formed in the lungs showing even examples of Rasmussen's aneurysm, which had been caused by catarrho-pyogenic organisms, to the exclusion of tubercle bacilli.

So far from catarrho-pyogenic infection being responsible only for the last signs and symptoms of a case of "pulmonary tuberculosis," they could alone produce all the signs and symptoms met with in this disease, quite independently of tubercle bacilli: indeed catarrho-pyogenic organisms might arrive in the respiratory tract as early as tubercle bacilli did, and it was due to their activity that all these characteristic changes were produced in the lung, which formerly were so aptly spoken of as consumption, and were now so erroneously attributed to pure tuberculous infection.

Three Cases of Bronchiectasis.

By L. S. T. BURRELL, M.D.

IN one case, artificial pneumothorax having failed, thoracoplasty was performed. The patient was still coughing up a large quantity of sputum, but her general condition was slightly improved.

In another case artificial pneumothorax had failed owing to adherent pleura; phrenicotomy was then performed and later thoracoplasty. The patient was a little less toxic but continued to cough up a quantity of offensive sputum.

The third case was undergoing treatment by artificial pneumothorax, and a series of X-ray films were exhibited to show the bronchiectatic cavities into which lipiodol had been injected.

Clinical Section.

President—Dr. G. NEWTON PITT, O.B.E.

Splenectomy for Essential Thrombocytopenic Purpura Hæmorrhagica in a Girl aged 10 years.

By BERNARD MYERS, C.M.G., M.D.

(WITH REPORTS BY RODNEY MAINGOT, F.R.C.S., AND A. KNYVETT GORDON, M.B.)

I.—Dr. BERNARD MYERS.

W. B., AGED 10, was admitted to the Royal Waterloo Hospital on July 12 last on account of bleeding from the mouth and nose. She had been treated previously in the out-patient department as a case of purpura.

Examination showed her to be a well-developed girl. There were numerous small areas in the body having the appearance of bruises, and many petechiæ. There was a slow, continuous oozing from the gums, mouth and nose. The gums were swollen until splenectomy was performed. Nothing of note was found in the lungs, heart or abdomen. A small amount of blood was present in the urine on one occasion. There was no history of melæna. Some joint-pains had been complained of (knees).

The disease had first been noted sixteen months previously. There is no similar case in her family. Patient has no brothers or sisters. She had previously suffered from measles twice, mumps and whooping-cough.

The appetite was good, there had been some vomiting, the bowels were constipated. The spleen was not palpable on admission, but it was distinctly felt on November 10. The temperature was generally normal, but occasionally there were slight rises of 1° F.; the pulse varied from 80 to 120, and the respirations 18 to 20 per minute. She was weighed on several occasions but the weight never varied from 4 st.

On July 16, 1925, Dr. Donaldson reported:—*Erythrocytes*, 4,900,000 per c.mm., hæmoglobin, 50 per cent.; colour index, 0·5. *Leucocytes*, 16,250 per c.mm. Differential count: Polymorphonuclears, 59 per cent.; lymphocytes, 38 per cent.; transitionals, 1 per cent.; eosinophils, 2 per cent. *Platelets were fairly numerous*. No abnormal erythrocytes were seen. The *coagulation time* was ninety seconds.

On October 3, 1925, the blood report was as follows:—*Erythrocytes*, 3,900,000 per c.mm.; hæmoglobin, 45 per cent.; colour index, 0·5. *Leucocytes*, 5,000 per c.mm. Differential count: Polymorphonuclears, 44 per cent.; lymphocytes, 53 per cent.; transitionals, 2 per cent.; eosinophils, 1 per cent. *No platelets were seen*. The erythrocytes showed anisocytosis and some were very pale, but were otherwise normal.

Dr. Knyvett Gordon, who is interested in this case, kindly examined this child's blood, and his report follows (p. 33).

As the usual treatment was quite unavailing, and a grave termination being always possible in this disease, one felt that the patient should be given the benefit of splenectomy, as excellent results, and indeed apparent cures, have been reported by George A. Minot and others in the United States and by Sutherland in England. It is first necessary, however, to make sure that the case comes within the category of

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those suitable for operation; the preliminary tests consist of: (1) the presence of thrombocytopenia, (2) prolonged bleeding time (as tried by a bayonet-pointed needle on the ear), (3) normal clotting time (the clot is, however, non-retractile), and (4) a positive capillary pressure-test (performed by applying a tourniquet or bandage around the arm with only moderate pressure for two to three minutes so that the flow of blood through the arteries is only slightly interfered with, when petechiæ appear on the limb). In our case the first, second and fourth conditions were present, the third test was not tried. This, therefore, being an essential and not a symptomatic case was suitable for splenectomy. Minot¹ states that since splenectomy was first performed for this disease by Kaznelson in 1916 over forty cases have been reported; that a number of patients have remained well over five years after operation, and that the operative mortality is about 5 per cent. Minot thus summarizes the position:—

"The immediate effects are to cause cessation of bleeding; a rapid increase in the numbers of blood-platelets, at times to above normal; the blood-clot to become retractile, and the bleeding time normal. Later, in from weeks to months, the blood-platelets usually decrease to well below normal and yet another bleeding does not recur."

This case being suitable for splenectomy, and the usual treatment by complete rest, administration of calcium salts, sera and blood transfusion having proved futile, I asked my colleague, Mr. Rodney Maingot, kindly to carry out the operation. His report is attached.

I must add that the almost dramatic cessation of all oozing from the moment the spleen was removed was remarkable, nor has there been any trace of bleeding since from the skin or any mucous membrane. The patient now looks the picture of health, and states that she never remembers feeling so well.

II.—MR. RODNEY MAINGOT, F.R.C.S.

I opened the abdominal cavity through an incision in the outer border of the left rectus muscle, commencing at the costal margin and terminating at the level of the umbilicus. The fibres of the rectus abdominis were divided longitudinally $\frac{1}{2}$ in. from its outer border. The spleen was delivered quite easily through this incision; the tail of the pancreas was identified and stripped mesially so that the individual vessels to the spleen could be clearly seen, secured and ligatured.

A Moynihan's mesenteric forceps was then applied to the vessels distal to the ligatures and the spleen was removed.

A splenecule the size of a hazel-nut was also removed.

The spleen was not adherent to the diaphragm and there was no intraperitoneal soiling with blood.

The peritoneum and the anterior sheath of the rectus were closed with a continuous suture of No. 2 twenty-day kalmariid catgut, and the skin approximated with a subcuticular stick of Japanese silkworm gut. Dr. W. E. Robinson, the anæsthetist, remarked, on the termination of the operation, that the hæmorrhage from the gums, which was profuse before splenectomy, ceased abruptly before the peritoneal suture was applied. I noted, too, that the skin wound bled profusely during the operation, but when I came to sew up there was no hæmorrhage. We can say, therefore, that splenectomy has an immediate effect in these cases, and that platelets are liberated in large quantities, which aid coagulation as soon as the spleen is removed.

The subcuticular stitch was removed on the tenth day. There was no subcutaneous hæmatoma, and the wound healed by first intention.

The patient made an excellent recovery; all hæmorrhages have ceased: and her general condition has improved beyond all recognition.

¹ *Boston Medical and Surgical Journal*, January, 1925.

It may be unwise to base too much on the successful issue of one case, yet the results in this *particular* case have been so excellent that I shall urge splenectomy in the case of all future sufferers from purpura hæmorrhagica.

III.—DR. KNYVETT GORDON.

In dealing with cases of purpura it seems to me important to distinguish between those in which the undue fluidity of the blood is due to toxic factors, i.e., toxic purpura, and those in which it is due to diminution of platelets, i.e., essential purpura, respectively. For the former splenectomy is not necessarily indicated, though as our knowledge advances it is possible that this may be the method of choice in some cases; for the latter it would appear to be the only available remedy for the cure of the disease as distinct from the alleviation of symptoms.

It is thus necessary in the investigation of any given case to exclude the toxic factor. Apart from the action of certain chemical poisons, e.g., benzole, toluene and aniline derivatives, with which we need not concern ourselves, for they do not present any difficulty in diagnosis, certain bacterial toxins may give rise to purpura. Of these, diphtheria is perhaps the best example, but the streptococci and the various bacilli of the *coli* group, and perhaps other hæmolytic organisms, should be tested for. I take it that these act by the production in excess of bacterial ferments and consequent hæmolysis.

As regards essential purpura, the keynote of the pathology is to be found in the work of Ledingham and Bedson. Ledingham (*Lancet*, June 13, 1914, p. 1673) prepared an anti-platelet serum, and found that when injected into guinea-pigs all the symptoms of essential purpura, including cutaneous and subcutaneous hæmorrhages and mucous surfaces, resulted. Subsequently, Bedson (see *Lancet*, November 29, 1924, p. 1117, and other papers) found that splenectomy in the guinea-pig afforded protection against the production of experimental purpura by the injection of anti-platelet serum.

In the case under discussion the findings are as follows:—

- (a) The urine showed no abnormality.
- (b) Neither in the fæces nor urine were any pathogenic bacteria found.
- (c) The blood showed slight leucopenia, with relative lymphocytosis; the red cells were not diminished, but the hæmoglobin was only 42 per cent. The details were:

November 5, 1925.

Red cells.	Anisocytosis	marked
	Poikilocytosis	marked
	Normoblasts	none
	Megaloblasts	none
	Total count	4,984,000 per c.mm.
	Hæmoglobin	42 per cent.
	Colour index	0·43
Average size of red cells not increased.		
White cells	Total count	4,800
	Polymorphs	30 per cent. equals 1,440
	Large lymphocytes	45 " " 2,160
	Small lymphocytes	15 " " 720
	Hyalines	2 " " 96
	Eosinophils	1 " " 48
	Mast cells	2 " " 96
	Leucoblasts	3 " " 144
Lymphoblastic plasma cells		2 " " 96

- (d) The bleeding time was prolonged from three minutes (normal) to twenty minutes.

The blood-platelets, however, were almost absent, only two being found in each film, occupying two-thirds of a 3-in. by 1-in. slide. Bedson's method was employed for collection of the blood, and the slide was stained with my modification of Pappenheim's panoptic stain. On a control slide from a normal person 300,000 platelets per c.mm. were seen.

In view of the high total red cell count and the absence of urgent symptoms, transfusion was not advised before operating and was not subsequently found necessary. The operation of splenectomy was performed with rapidity by Mr. Rodney Maingot, and resulted in no obvious shock. Subsequently daily observations were made on the blood, the results of which are recorded on the chart submitted. These may be summarized as follows:—

The day after the operation the platelets numbered 50,000 per c.mm., and steadily rose to a total of 390,720 per c.mm. on the eighteenth day. A slight fall in the red cell total count occurred, but this was of short duration, and ultimately the number of red cells rose to six and a half millions. After the operation a polynuclear leucocytosis occurred up to 26,000 per c.mm., gradually subsiding to 12,600 per c.mm. With the exception of a small percentage of myelocytes, of short duration, no primitive forms either of red or white cells were found. At first, scarcely any lymphocytes appeared in the blood, but ultimately the loss of these was made good. The bleeding time returned to normal the day after the operation and remained so. The spleen weighed 75 grm., and measured 4 in. by 2½ in. by 1½ in. Macroscopically, it could not be said to show any obvious abnormality, but on microscopical examination of portions fixed by the Helly-Maximow method, it was found that while the Malpighian bodies showed no abnormality, the endothelium of the pulpar sinuses was in marked proliferation, the lumina being stuffed with large cells, so that very few spaces were visible. Many of these cells were in a state of mitosis. The lymphocytes in the pulp were markedly diminished in number, their places being taken by the aforesaid active endothelial cells, many of which contained fragments of cells which may have been phagocytosed platelets. Without further observation and experiment, however, it is not, I think, possible to affirm this. The cells of the splenic pulp, however, are known to be phagocytic for red and white cells and probably for bacteria also. Cultures from the spleen were sterile, and the sections showed no free iron. Hæmolysis of red cells was not therefore excessive.

I submit that the investigations in this case are conclusive of essential as distinguished from toxic purpura.

When I first saw this case, I had not come across the paper by Sutherland and Williamson (*Lancet*, February 14, 1925, p. 323), recording the first two cases of splenectomy for essential purpura in this country. Subsequently, they gave details of previous cases on the Continent and America. The diagnosis in the case of some of the latter seems open to doubt, because it is very doubtful whether an accurate method of counting the platelets could have been employed, and also the duration of the disease in some of them was not more than four days. The findings in our own case tally very closely with those of Sutherland and Williamson, with the exception that I do not agree that non-retraction of the clot is an important feature in diagnosis. I have observed this phenomenon both in open and closed tubes of blood sent for agglutination tests, and for the Wassermann reaction, from cases in which there could not have been essential purpura. Since reading Sutherland and Williamson's paper I have kept notes of these specimens, and find that non-retraction of the clot is present in 40 per cent.

I would emphasize that in cases of essential purpura the spleen is not necessarily enlarged. This is in marked distinction from some of the cases of splenic anæmia with hæmorrhage from mucous surfaces, with which the disease may be confused, if an accurate examination of the blood is not made.

[January 8, 1926.]

Case of Large Lymphangioma or Telangiectasis occupying the Lower Half of Left Abdomen and Left Leg.

By W. A. MILLIGAN, M.D.

PATIENT, an infant, aged 1 year. The condition is entirely hemilateral and involves the segments from the eighth dorsal to the last sacral.

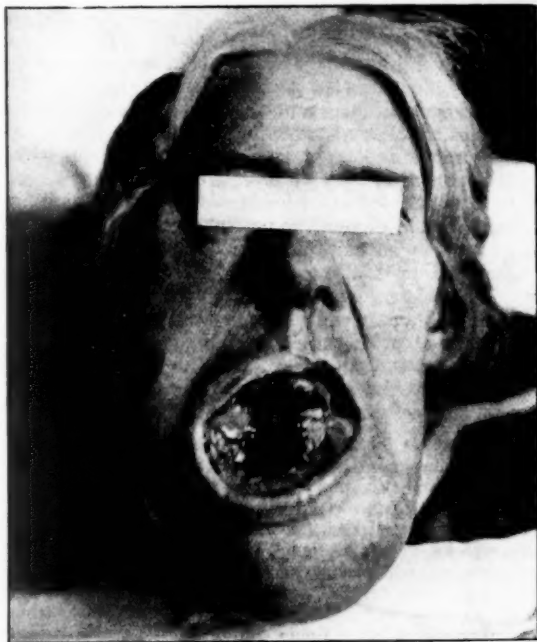
The condition is very like congenital elephantiasis. It has been treated by means of radium, large flat applicators, half strength, containing 4 rr. mg. radium bromide, screening $\frac{1}{16}$ mm. of lead with black paper and lint, exposure one and a half hours, and apparatus so arranged as to give cross-fire radiation.

Case of Sarcoma of the Right Lower Jaw.

By DUNCAN C. L. FITZWILLIAMS, C.M.G., F.R.C.S.

MRS. B. came to see me two years ago with a small growth attached to the right lower jaw. This was removed, and the section is shown. It was believed to be an epithelial odontome.

She was lost sight of for two years, when she was found to be in the present



condition. The growth now overlaps the bone for almost its whole extent. No glands are to be felt. The X-ray shows changes very like those of a periostosis sarcoma.

Difficulty is met with in nourishing the patient.

March 12, 1926.

A Case of Arthritis with Multiple Subcutaneous Nodules and Sclerodactylia.

By D. C. HARE, M.D.

MRS. H. P., aged 26, has suffered from joint trouble for about four and a half years. The onset was gradual and was not associated with any other illness nor with pregnancy. She has been getting gradually but not rapidly worse. From the first the hands have been liable to become cold and blue; she first noticed small lumps on her hands about two years ago. There is no history of serious illness; she has never had rheumatic fever or chorea or gastro-intestinal disturbance. She has had three pregnancies, but no living children; one miscarriage in the early months, and two premature births.

Present condition.—The general condition is poor, though wasting is not marked. The hands are always bluish, but become deeply cyanosed on exposure to cold. The skin over the fingers is atrophic and shiny. There is no marked deformity, but a general swelling and thickening of the tissues, and the movements of the hands are stiff, limited and painful. The wrists, elbows, shoulders, and temporo-maxillary joints are affected; also the knees, ankles and feet, but to a less extent. The patient complains of aching pains and stiffness, but there are no noticeable changes except the presence of nodules.

Nodules.—There are numerous small, subcutaneous nodules, closely resembling the rheumatic nodules seen in children. They occur about the metacarpo-phalangeal joints, the dorsal tendons of the hands, and the flexor tendons of the wrist. They are numerous on the elbow-joints, and occur in small numbers on the knees and ankles. One is present on the front of the right tibia, about three inches below the knee. Along the tendons the nodules are very small, about the size of hempseed, and look like a string of beads. In other situations they vary up to $\frac{1}{4}$ in. across. They are painful and tender at times. They have not altered appreciably during the six months that the patient has been under observation, although the patient's general condition has improved.

The Heart.—Appears to be quite normal. A soft, localized systolic murmur is sometimes heard, not conducted into the axilla.

Focal Sepsis.—The patient has been fully investigated for focal sepsis and none found. The urine, genital tract, bowel, naso-pharynx, and mouth have yielded nothing abnormal. Wassermann reaction negative. No rise of temperature when under observation in hospital.

Remarks.—The case is shown with the provisional diagnosis of rheumatoid arthritis with trophic changes of the skin of the fingers and multiple fibrous nodules.

Dr. F. PARKES WEBER thought the condition of the patient's hands was characteristic of an early stage of diffuse symmetrical scleroderma "of the sclerodactylia type." The hands were turgid, more or less livid, with shiny skin over slightly bent and stiff fingers. This was the condition of patients with the atrophic and scar-like fingers of advanced sclerodactylia sometimes described as having preceded the cicatricial, advanced stage of the disease. It had often been confused with Raynaud's disease. The present patient also had lines or rows of small fibrous nodules about the extensor tendons at the backs of the hands, and larger subcutaneous nodules at the elbows especially over the olecranons. The latter probably contained calcareous deposits.¹ It would be interesting to have these and all the other nodules examined by X-rays to ascertain which (if any of them) contained calcareous material. Thyroid treatment might be tried together with, or before, the treatment by diathermy, which had been proposed by Dr. Hare.

¹ For the literature on the fibrous nodules and calcareous concretions occurring in association with, or without, scleroderma, see F. Parkes Weber, *Urologic and Cutaneous Review*, St. Louis, 1923, xxvii, p. 409.

Three Cases of Splenectomy for Essential Thrombocytopenic Purpura Hæmorrhagica.

Shown by BERNARD MYERS, C.M.G., M.D., RODNEY MAINGOT, F.R.C.S., and A. KNYVETT GORDON, M.B.

THESE three cases of essential thrombocytopenic purpura hæmorrhagica were recently admitted as in-patients to the Royal Waterloo Hospital. All three had shown well-marked crops of petechiæ in the skin and buccal mucous membrane, and in all the blood-platelets were either absent or greatly reduced in number, the bleeding time was increased, and the capillary resistance test showed a good crop of purpuric spots in two minutes. The retraction of the blood-clot was not tried, as Dr. Knyvett Gordon was of opinion that it was not definitely diagnostic of this disease. The spleen was enlarged in one case. The ordinary treatment by calcium salts, sera and transfusion of blood (although of some temporary value in two cases) failed to stop the hæmorrhages, and the prognosis having always the possibility of a grave termination it was determined to perform splenectomy in each case. Although no further hæmorrhage has occurred in any of the cases up to the present it is obviously far too soon to judge of the effectiveness of the operation. It is hoped, therefore, to show these cases again before the Section in a year's time and report progress. Two of the patients, Mrs. E. D., aged 29, and W. B., have previously been shown before the Section, and accounts of these cases given in the *Proceedings* of this Section. In none of these cases could we obtain a history of any other member of the family suffering from this disease.

Case I.—E. D., aged 29, married, two children. First attack of purpura occurred when she was 12 years of age, and was acute. She suffered from no further attack until she was 24 years old, when, after the birth of a child, she suffered from uterine hæmorrhage in the form of continuous oozing, which lasted for four weeks, and the efforts of the gynecologists to stop it were quite unavailing. At the same time, her skin was covered with petechiæ, which were also present in her mouth, and to a less extent in her nose; from both of the latter there was oozing of blood. All the usual methods of treatment, calcium salts, styptics, sera, &c., quite failed to stop the bleeding, while the temperature rose to 104° F., and the red blood-corpuscles fell to 2,000,000. In the blood only an occasional platelet was seen. Transfusion of blood from a suitable donor, citrated 0.25 per cent., however, stopped the bleeding for the time being, and she left hospital in a few weeks free from any sign of purpuric rash and in fairly good health.

Before long a fresh purpuric rash made its appearance on the arms, legs, and mouth; it lasted about a week and was followed by recovery. Since then numerous similar attacks have occurred, and she has been three times admitted to hospital for menorrhagia, which seemed to be due to the purpuric state. After the last attack it was considered advisable to carry out splenectomy, as this operation has been fully justified for this kind of purpura in U.S.A. and by Sutherland in England. The operation was accordingly performed on January 15 last.

It so happened that before the operation she had been free from any sign of purpura for three weeks, and her red blood-cells numbered 6,504,000 per c.mm., and the platelets 60,000. The bleeding time, which was fifteen minutes before operation, was two minutes (normal) to-day. The capillary resistance test before operation showed a crop of purpuric spots in two minutes; on several occasions since the operation no purpuric spots were visible even after five minutes.

Dr. Knyvett Gordon's report of his pathological investigations is appended.

REPORT ON CASE OF MRS. E. D., JANUARY 13, 1926.

By A. KNYVETT GORDON, M.B.

Urine.—Appearance, amber colour, slightly cloudy; specific gravity 1.016; reaction acid; albumin absent; sugar absent; blood absent. Centrifuged deposit: Many squamous epithelial cells, some leucocytes and a few red blood-cells present. No casts, no crystals. No tubercle bacilli. Cultures sterile.

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Blood.—Red cells: No histological abnormality. Total count 6,504,000 per c.mm.; hæmoglobin 60 per cent.; colour index 0.5. White cells: Total count 9,000 per c.mm.; polymorphs 65 per cent., large lymphocytes 15 per cent., small lymphocytes 15 per cent., hyalines 3 per cent., eosinophils 2 per cent. Platelets 60,000 per c.mm.

Investigations made at time of Splenectomy January 15, 1926.

First Count, just after Abdominal Incision.—Red cells 6,680,000 per c.mm.; white cells 17,200 per c.mm.; platelets 33,000 per c.mm.; polymorphs 75 per cent., large lymphocytes 10 per cent., small lymphocytes 10 per cent., hyalines 3 per cent., eosinophils 2 per cent.

Second Count, during Sewing up.—Red cells 6,220,000 per c.mm.; white cells 25,400 per c.mm.; platelets 124,000 per c.mm.; polymorphs 80 per cent., large lymphocytes 8 per cent., small lymphocytes 8 per cent., hyalines 2 per cent., eosinophils 2 per cent. Splenic artery: Platelets 325,000 per c.mm. Splenic vein: Platelets 65,000 per c.mm.

January 17, 1926.—Red cells: No histological abnormality. Total count 4,920,000 per c.mm.; hæmoglobin 70 per cent.; colour index 0.7. White cells: Total count 27,000 per c.mm.; polymorphs 60 per cent., large lymphocytes 10 per cent., small lymphocytes 15 per cent., hyalines 4 per cent., eosinophils 1 per cent., myelocytes 6 per cent., metamyelocytes 4 per cent. Platelets 197,000 per c.mm.

January 21, 1926.—Red cells: No histological abnormality. Total count 6,372,000 per c.mm.; hæmoglobin 76 per cent., colour index 0.6. White cells: Total count 9,200 per c.mm.; polymorphs 70 per cent., large lymphocytes 10 per cent., small lymphocytes 15 per cent., hyalines 3 per cent., eosinophils 2 per cent. No histological abnormality. Platelets 318,000 per c.mm.

Histology.—A portion of liver removed at operation showed no histological abnormality. The spleen was of normal size and weight and showed on section no obvious macroscopical abnormality. Portions were fixed in Helly-Maximow fluid and stained with iron hæmatoxylin and eosin, and also especially for hæmatogenous cells. The Malpighian bodies were normal in size and distribution, but the sinuses of the splenic pulp showed *excessive proliferation of endothelial cells*, many of which were in mitosis. There was no excess of fibrous tissue, and the capsule and trabeculae showed no abnormality.

Conclusion.—This is evidently a case of essential, not toxic, purpura in a quiescent interval.

A matter of distinct interest was the investigation of the platelets from blood obtained from the splenic artery and vein respectively; in the former there were 325,000, and in the latter 65,000 per c.mm. This investigation was made immediately before clamping the vessels. It will be noted how the blood-platelets increased in number after the operation.

Case II.—W. B., aged 10. As a full account of this case in which splenectomy was performed on November 13, 1925, has already been given¹ it is unnecessary to say more than that so far she remains quite free from any signs of purpura. She states that she feels in perfect health, a statement which is corroborated by her mother. Her blood-platelets are at the present time 479,200 per c.mm., and the bleeding-time, previously twenty minutes, is now less than two minutes. The capillary resistance test which before operation showed a crop of purpuric spots in two minutes now shows no purpuric spots in five minutes.

Case III.—A. W., aged 6, was admitted to the Royal Waterloo Hospital, early in February, having suffered from purpura hæmorrhagica for a month. There was no history of previous attacks.

He had had measles and chicken-pox as a baby but had suffered from no other illnesses.

There is no history of any similar case in the family. The child was very pale and suffered from bleedings from the gums and bowel. Some petechiæ were present on the arms, legs, and palate, and hæmorrhages occurred from the mouth. No blood-platelets were visible in the field before the operation of splenectomy on February 5 last. Since the operation the blood-platelets have numbered 250,000, while to-day they were over 1,000,000. The bleeding-time before the operation was fifteen minutes; at present it is five minutes. The capillary resistance test before operation showed a crop of purpuric spots in two minutes; at present no spots are produced after four and a half minutes. A sample of blood was taken

¹ See *Proceedings*, 1926, xix (Clin. Sect.), p. 31.

from the splenic artery and vein immediately after pedicle was clamped and spleen removed. The platelets in the former number 168,000 per c.mm. and the latter 56,000.

Dr. Knyvett Gordon's pathological report on the case is appended:—

A. W.—ESSENTIAL PURPURA.

REPORT BY A. KNYVETT GORDON, M.B.

Blood, January 23, 1926.—Red cells: No histological abnormality. Total count, 3,256,000 per c.mm.; hæmoglobin, 55 per cent.; colour index, 0·9. White cells: Total count, 5,600 per c.mm.; polymorphs, 45 per cent.; large lymphocytes, 20 per cent.; small lymphocytes, 25 per cent.; hyalines, 2 per cent.; eosinophils, 1 per cent.; Türk cells, 4 per cent.; myelocytes, 2 per cent. Platelets: none seen.

Observations at Operation. Splenectomy, February 5, 1926.

Before Operation, during Anæsthesia.—Red cells: No histological abnormality. Total count, 5,584,000 per c.mm.; hæmoglobin, 55 per cent.; colour index, 0·5. White cells: Total count, 37,600 per c.mm.; polymorphs, 20 per cent.; large lymphocytes, 30 per cent.; small lymphocytes, 35 per cent.; hyalines, 5 per cent.; eosinophils, 1 per cent.; plasma cells, 9 per cent. Platelets: none seen.

Blood from Splenic Artery.—Platelet count, 168,000 per c.mm.

Blood from Splenic Vein.—Platelet count, 56,000 per c.mm. Both the foregoing taken immediately after pedicle was clamped and spleen removed.

Capillary Blood after Operation.—Red cells: No histological abnormality. Total count, 5,180,000 per c.mm.; hæmoglobin, 55 per cent.; colour index, 0·5. White cells: Total count, 37,800 per c.mm.; polymorphs, 20 per cent.; large lymphocytes, 30 per cent.; small lymphocytes, 35 per cent.; hyalines, 5 per cent.; eosinophils, 1 per cent.; plasma cells, 9 per cent. Platelets: 104,000 per c.mm.

Blood, February 9, 1926 (Fifth Day).—Red cells: Anisocytosis, marked; poikilocytosis, marked; punctate basophilia, distinct; polychromasia, distinct; total count, 2,550,000 per c.mm.; hæmoglobin, 40 per cent.; colour index, 0·8; nucleated red cells, 2,800 per c.mm. White cells: Total count, 5,400 per c.mm.; polymorphs, 20 per cent.; large lymphocytes, 25 per cent.; small lymphocytes, 45 per cent.; hyalines, 3 per cent.; eosinophils, 0; myelocytes, 4 per cent.; leucoblasts, 3 per cent. Platelets: 204,000 per c.mm.

Spleen.—The Malpighian bodies are normal. The splenic pulp is an irregular mass of proliferating cells distending the sinuses so that their outline is almost lost. These are seen to be endothelial cells derived from the lining of the pulpar sinuses. Many are in mitosis. Very few erythrocytes, and less than the normal number of lymphocytes are present.

The small lieno-gastric gland showed no histological abnormality.

Blood.—February 13, 1926. Red cells: Anisocytosis, marked; poikilocytosis, marked; punctate basophilia, distinct; polychromasia, distinct; total count, 4,970,000 per c.mm.; hæmoglobin, 40 per cent.; colour index, 0·4; nucleated red cells, 2,200 per c.mm. White cells: Total count, 11,600 per c.mm.; polymorphs, 70 per cent.; large lymphocytes, 5 per cent.; small lymphocytes, 10 per cent.; hyalines, 3 per cent.; eosinophils, 2 per cent.; myelocytes, 5 per cent.; metamyelocytes, 5 per cent. Platelets, 250,000 per c.mm.

MR. RODNEY MAINGOT, F.R.C.S.

Splenectomy may be a very simple operation, or may present difficulties which are insuperable. Everything depends on the adhesions which bind the spleen to the parts around. In some cases these adhesions are very few and slender, whilst in others the organ appears to be fused to the diaphragm and to the adjacent structures. Now in our three cases of essential thrombocytopenic purpura hæmorrhagica the adhesions in all were few and thin; and the operation presented no technical difficulties. I employed an incision placed over the junction of the middle and outer one-third of the left rectus in its upper half. The muscle-fibres were split longitudinally and the peritoneum exposed.

Tetra cloths were clipped to the everted muscle-edges before opening the abdominal cavity. The full delivery of the spleens through the incisions and the ligaturing of the pedicles (by the three-clamp method) were all accomplished with speed and ease. By tightly packing large Cripps's pads, wrung out in hot salt solution, into the splenic beds, all oozing from here could be controlled or arrested whilst the spleens were being removed. The splenic pedicles were tied off with No. 3 thirty-day catgut; the other vessels were ligatured with No. 1 catgut or

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No. 2 Pagenstecher thread ; the peritoneum and the rectus sheath were closed in each case with a continuous suture of No. 2 catgut ; and the skin edges approximated by subventricular stitches.

In one case (Case I) a splenecule, the size of a marble, was present, and was removed after ligaturing the large artery that supplied it.

In our second case, acting on Dr. Myers' suggestion, I removed a small portion of the liver and an epiploic gland for microscopical investigation. The subsequent report on these tissues showed them to be normal in structure. In Case II, I isolated the splenic artery and splenic veins, and collected 5 c.c. of blood from each. The blood from the artery contained 12 per cent. more thrombocytes than the blood from the veins. The time taken over these operations varied from ten to twenty minutes. From observations during operation on these three cases I am led to believe that splenectomy has an instantaneous effect in arresting hæmorrhages from the mucous surfaces and into the skin. In our first case, Dr. W. E. Robinson, the anæsthetist, reported that the bleeding from the gums, which was profuse, proved to be very troublesome during the induction of the anæsthetic and right up to the point when the spleen was removed. As soon as the splenic pedicle was tied the hæmorrhage from the gums stopped with dramatic abruptness. In Case III, the free and uncontrollable oozing from the skin edges ceased as soon as the forceps were applied to the pedicle of the spleen.

It has been suggested that this phenomenon might have resulted from the shock produced by the operation. As there were no signs or symptoms of shock both during or immediately following these operations, this suggestion is difficult to uphold. Surely, a more likely determining factor is the massive and unhampered liberation of thrombocytes into the circulation following close upon the ablation of the spleen.

In our cases the patients passed through uncomplicated convalescences ; no fresh hæmorrhages have been reported in any of the three cases, and the results, so far, have been most gratifying in every respect. I share Professor Leschke's confidence that splenectomy is the correct treatment for *all cases* of essential thrombocytopenic purpura hæmorrhagica, whether the cases are of the *acute* or of the chronic relapsing types. It is generally agreed that ablation of the spleen is the best treatment for the chronic condition ; but I maintain that it is more urgently indicated for the *acute* types of the disease, as medical treatment, blood-transfusion, &c., have no effect whatever in arresting or even ameliorating the factors which determine the fatal issue.

A Case of Hemihypertrophy.

By C. F. T. EAST, B.M.

THE patient is a girl nearly 18 years of age. She is very tall and particularly long in the legs (fig. 1).

About five years ago it was noticed that the left leg was larger than the right, and she had a good deal of pain in the foot. Since birth it has been noticed that the face has been rather asymmetrical.

At the present time one may say that the whole of the left side of the body is larger than the right. The difference in size is most noticeable in the face and the legs. In the face the left side is distinctly longer than the right. This is well shown in the two photographs (figs. 2 and 3), one of which is composed of the right side of the face only, the negative being bisected and reversed to form the "left" side, and the other of the left side of the face only. The left side of the tongue is clearly larger than the other.

The left arm is half an inch longer than the right, and there is some asymmetry in the length of the fingers.

The left leg is nearly two inches longer than the right, and the left calf is an inch the greater in circumference. The tissues of the lower part of the left leg have a doughy, brawny character that does not signify cedema. There is marked capillary stasis in the legs and there are some early varicose veins around the left ankle. The left foot is about an inch longer than the right. She has very marked pes planus on both sides, more marked, apparently, in the left than in the right foot.

All over the body is a very fine capillary nævus; this is most marked on the hands, forearms, and trunk. On the legs the general capillary engorgement rather obscures it. This was present at birth.



FIG 1.

Family history negative. Patient otherwise normal and rather exceptionally intelligent.

It was thought that it might be possible to find some derangement of the pituitary body to account for the condition. Tests, however, yield negative results. Sella

turcica normal. Wassermann reaction negative. Blood-sugar curve and basal metabolic rate normal. Skiagram of the bones does not reveal any difference in their structure on either side.

The cause of this abnormality is wholly obscure. It evidently dates from birth but it is interesting to note that the increase in size of the left leg has only been noticed since puberty, that is to say, since the period of rapid growth has commenced. Growth has undoubtedly accentuated a condition that was previously present.

If the right side of the body were as large as the left, one would at once regard the condition as due to a pituitary defect. But it is difficult to conceive an endocrine

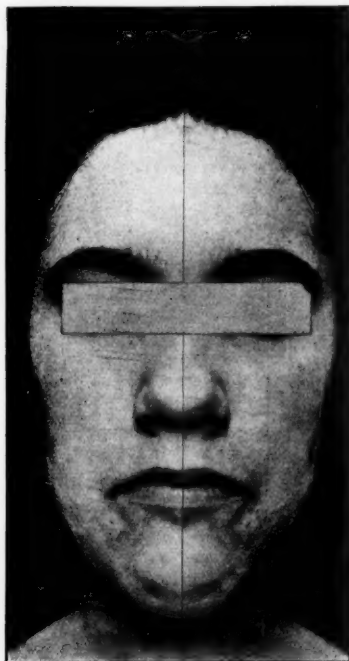


FIG. 2
Composite photograph from two left
halves of face.

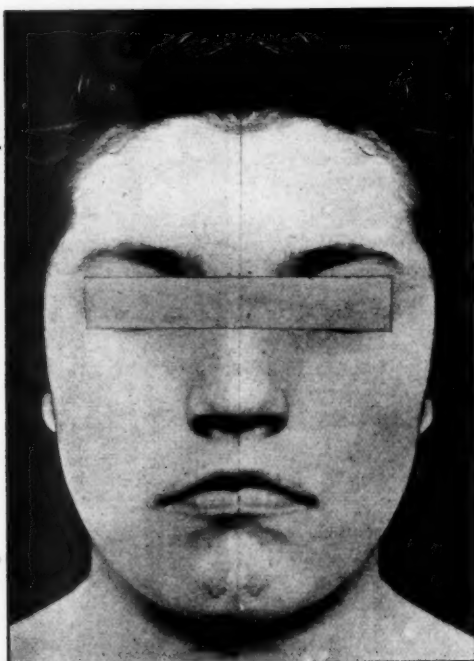


FIG. 3
Composite photograph from two right halves
of face.

derangement affecting one side of the body only. Perhaps her condition should be regarded as an exaggeration of the slight asymmetry that can be found in almost anyone. The amount of symmetry in the ordinary individual is rather astonishing than otherwise; the "awful symmetry" of the tiger certainly impressed the poet Blake. But such asymmetries as do occur are only found as a rule in one organ or limb, and do not include the whole of one side of the body. One must go back to a very early stage in development to explain this abnormality. The presence of a second congenital abnormality in the form of the generalized naevoid condition is also noteworthy.

[March 12, 1926.]

Case of Congenital Cyanosis.

By BERNARD MYERS, C.M.G., M.D.

FURTHER NOTE, AND ANATOMICAL REPORT BY SIR ARTHUR KEITH, F.R.C.S.,
F.R.S., ON CASE REPORTED IN THE *Proceedings* (CLINICAL SECTION),
1926, VOL. XIX, pp. 3—4.

D. F., AGED 6, was readmitted to the Royal Waterloo Hospital on January 27 last on account of bronchitis following whooping-cough.

The patient was very cyanosed on admission and the conjunctivæ were purple. Respiration was very rapid. There was no definite dullness. Moist râles were present all over the chest. She suffered from severe paroxysms at intervals. The heart's action was very rapid. No murmurs were heard. The cyanosis became extreme and the child died quite suddenly on January 29.

The necropsy was made by my house physician, Dr. Hewlett. The body was well nourished, but very cyanosed. The superficial veins were found to be greatly engorged when the tissues were incised. The organs were of a dark purple colour.

The heart was normally placed. The pericardium contained an increased amount of clear fluid. No valvular disease was seen.

The blood in the carotid arteries was distinctly dark coloured.

The lungs showed a firm adhesion at the left apex and base. There was a small cavity containing caseous material at the left apex. There was nothing else of importance in the lungs except signs of moderate recent bronchitis.

The liver was mottled.

A caseous gland was found in the mesentery.

Sir Arthur Keith kindly examined the heart (which is now in the museum of the Royal College of Surgeons) and reported as follows, illustrating his remarks with a drawing:—

DESCRIPTION OF HEART, BY SIR ARTHUR KEITH, F.R.C.S., F.R.S.

THIS heart shows a series of uncommon malformations, the chief of which are:—

(a) The bulbus element, infundibulum (fig., F) is expanded only to a minor degree; in systole its outer wall must have contracted against its inner or septal wall, and thus have occluded the pulmonary orifice.

(b) The valves of the pulmonary orifice, three in number, one being small in size, have fused or coalesced in the process of development so that the orifice is completely occluded. No blood could have passed from the right ventricle into the pulmonary artery.

(c) The pulmonary artery is thin walled, its lumen being 5 mm. in diameter, one-half the normal size.

(d) The only vessels which carried blood into the lungs were three small arteries, each about 1 mm. in diameter, which arose from the descending aorta and apparently represented the bronchial arteries. It is possible that the branches may also have passed into the lungs from intercostal arteries which, however, had not been preserved.

(e) The pulmonary veins are normal in number, but smaller in size than is usual. The left auricle is small, and the left ventricle is of less capacity than the right, but the wall of both right and left ventricle has the same thickness at the base, namely, 10 mm.

(f) The ductus arteriosus is absent; there is no trace of it.

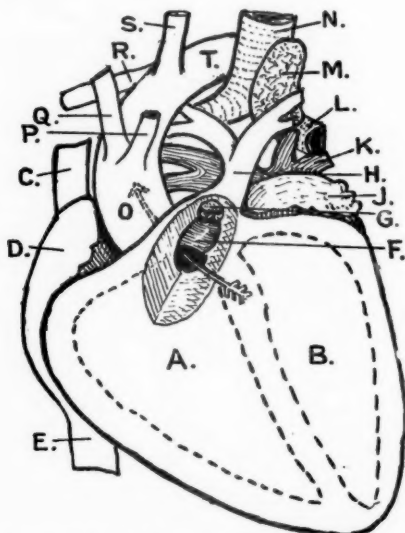
(g) This is due to the fact that the arch of the aorta has been formed out of the fourth right aortic arch in place of the fourth left, to which the ductus arteriosus has its normal attachment.

(h) Owing to the persistence of the right aortic arch, the great branches of the arch arise in an anomalous sequence (see fig., P, Q, R, S).

(i) The right auricle is hypertrophied, its walls measuring 3 to 5 mm., but its venous tributaries are arranged as in the normal heart.

(j) The ascending aorta has a diameter of 15 mm., and its orifice is situated over both ventricles, being placed above a widely patent interventricular orifice. Both ventricles therefore pumped all the blood which reached the heart through the systemic and pulmonary veins into the systemic aorta. The arch of the aorta, as it passes over the right bronchus, has a diameter of 10 mm.

This case shows that life is possible when only a small fraction of the blood passes



A. right ventricle; B. left ventricle; C. superior vena cava; D. right auricle; E. inferior vena cava; F. bulbus or infundibular chamber laid open; the arrow passes through the orifice of this chamber, then through the interventricular foramen to enter the aorta; G. pulmonary valves united developmentally; H. pulmonary artery; K. left pulmonary veins; L. left bronchus; M. large lymphatic gland; N. trachea; O. aorta; P. left carotid artery; Q. right carotid artery; R. right subclavian artery; S. left subclavian artery; T. arch of aorta.

through the lungs. The three bronchial arteries could not have carried a tenth of the blood which it is possible for pulmonary arteries to carry to the lungs in a normal heart.

The primary lesion in this case may be attributed to a coalescence of the pulmonary valves during the process of development, or to a failure in the developmental expansion of the bulbus cordis. It is likely that both lesions result from a common cause.

Clinical Section.

President—Dr. G. NEWTON PITT, O.B.E.

Case of Achondroplasia with Unusual Features.

By F. E. SAXBY WILLIS, M.D.

I. B., FEMALE, aged 12. Height 38 in. The long bones show the typically arrested development. The head is typically bradycephalic, the circumference being 22 in. Upper extremities show marked limitation of flexion, due to a failure to develop on the part of the upper epiphyses of the radius and ulna, both of which show in the radiogram reproduced very marked deformity (fig. 1). The hands are short

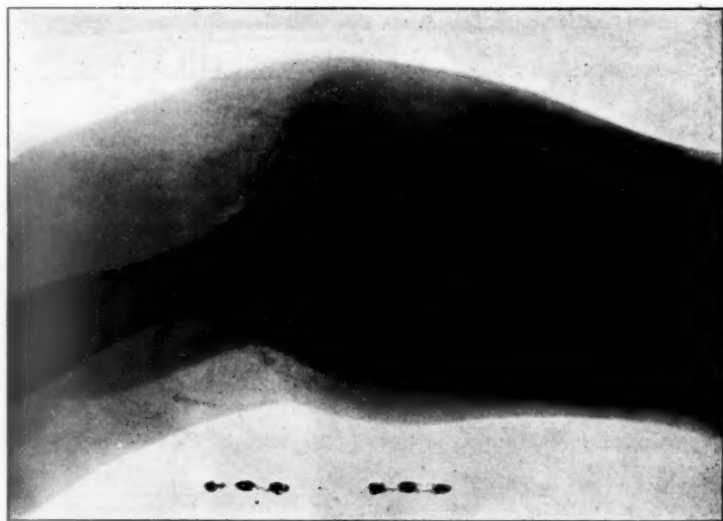


FIG. 1.

and stumpy, but an interesting feature is the atypical form of trident hand exhibited in the left hand, the diverging fingers being the middle and index, instead of the usual ring and middle fingers. This is shown in the accompanying radiogram (fig. 2, p. 2). The lower extremities show an unusual degree of bowing of the tibia and fibula, with very marked talipes equino-varus. The chief feature of interest, however, is the very marked kyphosis of the dorsal spine, instead of the usual lordosis. The musculature is well developed, and the child can perform simple acrobatic feats with ease.

46 Saxby Willis: *Achondroplasia*; Price: *Auriculo-Ventricular Block*

The family history is interesting. The patient is one of nine children, of whom none of the others are achondroplasiacs, but there have been several miscarriages. The Wassermann reaction in both the child and the mother is negative.



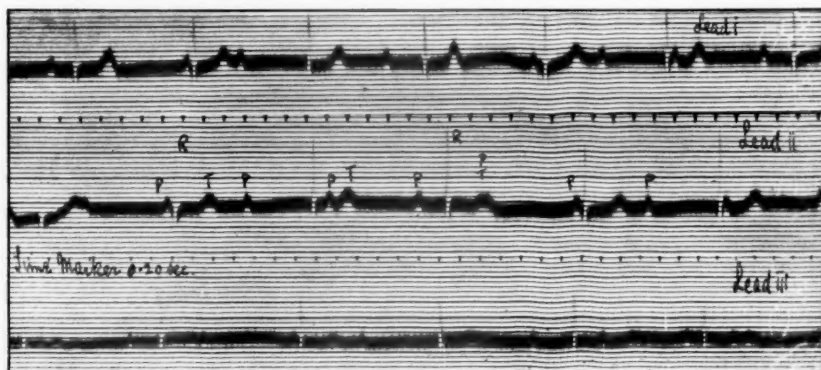
FIG. 2.

[May 14, 1926.]

Congenital Auriculo-Ventricular Block in a Child aged 5½ years.

By FREDERICK W. PRICE, M.D. (shown by B. PARSONS-SMITH, M.D.).

F. S., MALE, aged 5½; always rather undersized; anorexia on and off since infancy; late in walking; easily tired, but not breathless with ordinary exertion; no syncopal or epileptiform attacks; no cyanosis. Slight attack of whooping cough, December, 1924, but otherwise past history negative.



Physical State.—A moderately healthy-looking child; chest somewhat pigeon-shaped; no cyanosis; no clubbing of fingers; pulse-rate varies from 40 to 50, and rarely 60, per minute, is regular and of moderate size; systolic blood-pressure 110 mm., and diastolic 70 mm.

Force of apex impulse increased. Systolic murmur over whole præcordium with seat of maximum intensity at apex; short diastolic (early) murmur at apex, and occasionally at pulmonary area.

X-ray examination, left border $\frac{3}{4}$ in. outside nipple line, and right border $1\frac{1}{4}$ in. to right of sternum; thus the heart is enlarged on both sides.

The electrocardiogram (see fig. p. 46) shows complete auriculo-ventricular block.

Discussion.—Dr. B. PARSONS-SMITH (in introducing the case for Dr. Price) remarked upon the rarity of complete heart-block in young children, and suggested that such a condition might be associated with damage to the junctional tissues produced by (1) acute or chronic infection, (2) congenital malformation, or (3) the presence of a tumour. The past history excluded severe infection and rheumatism in any of its usually declared forms; in fact, the child had been practically free from disease of any kind except for a mild attack of whooping cough at the age of 4 years, so that there appeared to be no grounds for assuming the condition to be the outcome of infective processes. On the other hand, congenital malformation could not be excluded; although the typical syndrome of congenital heart disease did not appear in the present case, there was very definite cardiac enlargement, especially to the right, murmurs both systolic and diastolic, which did not readily admit of interpretation, were present, and the boy was certainly backward in physical development.

A number of cases of heart-block, associated with congenital heart disease, had been observed [1 and 2], and the speaker referred to a case of considerable interest recently recorded by Wilson and Grant [4], in which malformation of the heart with partial heart-block had been confirmed by autopsy and critically discussed from the pathological point of view.

In conclusion, he (Dr. Parsons-Smith) said he wished to emphasize two important features with regard to complete heart-block in children and young adults, viz: (1) that the ventricular rate was as a rule higher (40-50) than that observed with complete block in patients of more mature age, and (2) that the effective range of ventricular rate had definitely wider limits in juvenile cases of complete heart-block compared with the moderately inflexible bradycardia which characterized the condition in the more elderly and senile patients.

Dr. J. W. CARR (Chairman) briefly discussed the case from the ætiological point of view, and referred to the possibility of latent rheumatic infection; in his opinion, the case was one of mitral stenosis with heart-block. He inquired of Dr. Parsons-Smith whether complete heart-block in rheumatic children was observed with any frequency; also whether a Wassermann test had been taken in the case at present under discussion.

Dr. G. A. SUTHERLAND remarked upon the rarity of heart-block in children, and mentioned a communication by Dr. Whipham [3], in which the earliest cases of congenital heart disease with dissociation were recorded. He regarded the present case as one of congenital heart disease, and emphasized the right-sided cardiac enlargement and also the well-recognized association between patency of the interventricular septum and developmental anomalies of the junctional tissues secondary thereto. In his opinion, rheumatic infection never gave rise to permanent heart-block in children. He further suggested that the case should be very carefully considered with regard to prognosis and treatment; the latter would be thought not to be required to any great extent, for his impression was that patients in cases of this nature should be encouraged to lead, as far as possible, a normal mode of life.

Dr. BERNARD MYERS said that in his opinion the physical signs and the past history of the child were strongly in favour of congenital rather than acquired disease. He remarked upon the range of the pulse-rate which, taken at rest, was frequently over 50, and asked Dr. Parsons-Smith whether it was usual to find comparatively high ventricular rates in older children (10 to 14 years of age) and young adults suffering from complete heart-block.

Dr. ABRAHAMS agreed that the child should be encouraged to lead, as far as possible, a normal mode of life, and inquired whether any definite conclusions had been arrived at with regard to the question of exercise tolerance. He assumed that the pulse-rate figures (40-60) represented counts taken during observation at hospital, irrespective of any reference to effort

tests. The latter might be, he thought, definitely helpful in cases of heart-block; and he would be glad to know if Dr. Parsons-Smith had made any observations in this respect.

Dr. PARSONS-SMITH (in reply) said that he had no definite knowledge of complete heart-block rheumatic in origin in young children, and would regard it as an extremely rare occurrence. A Wassermann test had not been performed, and, although the child had none of the typical stigmata of congenital syphilis, he thought that it would be advisable for this to be done. He entirely agreed with Dr. Sutherland's confirmatory remarks in regard to the case being one of congenital disease, and with his suggesting that the child's future life should be developed on natural lines without restriction. He (Dr. Parsons-Smith) said that in his opinion complete heart-block in children and in young adults was, as a rule, associated with a comparatively high ventricular rate (50 or over) and a slight range of variation to natural stimulation, exercise emotion, &c.

In reply to Dr. Abrahams, he said he thought that there was a definitely deficient exercise tolerance in all cases of complete heart-block, and that the disability, as such, would be intensified in proportion to the degree of the bradycardia, and also the presence or absence of co-existing cardiac disease, congenital or acquired.

REFERENCES.

- [1] CARTER, E. P. and HOWLAND, J., *Johns Hopkins Hosp. Bull.*, 1920, xxxi, 351-354. [2] ROMBERG, E. C., and WHITE, P. D., *Boston Med. and Surg. Journ.*, 1924, cxc, 591-592. [3] WHIPHAM, T. R., *Brit. Journ. Child. Dis.*, Nov., 1915, xii, pp. 321-327. [4] WILSON, J. G., and GRANT, R. T., *Heart*, 1926, xii, 295-305.

Stenosis of the Anus in Infants.

By BERNARD MYERS, C.M.G., M.D.

AMONG 1,750 children who have attended the Children's Clinic, there have been five who have suffered from stenosis of the anus.

The symptom complained of by the mother in each case was constipation from birth, which, even with the frequent use of laxatives, persisted so that the bowels were only opened every two to four days, or less frequently. In three of the cases there was vomiting also, and in two convulsions. All the symptoms were immediately relieved after the anus was dilated.

The ages of the infants when brought for treatment varied from three weeks to ten weeks.

One child aged three weeks had not had an action of the bowels for the previous eight days, and was suffering from severe convulsions. Immediately the anus was dilated a large motion was passed and the convulsions ceased. This child has remained well since and the bowels have been open daily.

In none of these cases has there been a return of the symptoms after dilatation, and it is over four years since the first case was seen. It has been our practice to give liquid paraffin, half a teaspoonful daily, for the first week after the parts were stretched, and then to stop it altogether; but I am not at all sure that any paraffin is required.

I incline to the opinion that some, or perhaps all, of these cases, if left untreated, would become victims of chronic constipation and ill-health. Last year I saw a woman aged 45 who had suffered from constipation all her life, and, according to the statement of her mother, it dated from birth. On examination, the cause of the constipation was found to be stenosis of the anus, but, contrary to one's experience from the infants mentioned above, she was not cured by dilatation, although I believe she would have been had she been treated during infancy.

The following are briefly the histories of two of the cases:—

Case I.—S. W., boy, aged 4 years and 4 months, was taken to the Children's Clinic when 7 weeks old on account of being constipated since birth. The bowels had not been opened for the previous four days. The boy had been breast fed. There had been vomiting and convulsions.

No other cause of the constipation being apparent the anus was examined and found to be stenosed. It was gently dilated, a large motion being immediately passed. The vomiting and convulsions ceased; the bowels were opened daily during the next fortnight and have continued to give no further trouble, although no laxative or other medicine has been required.

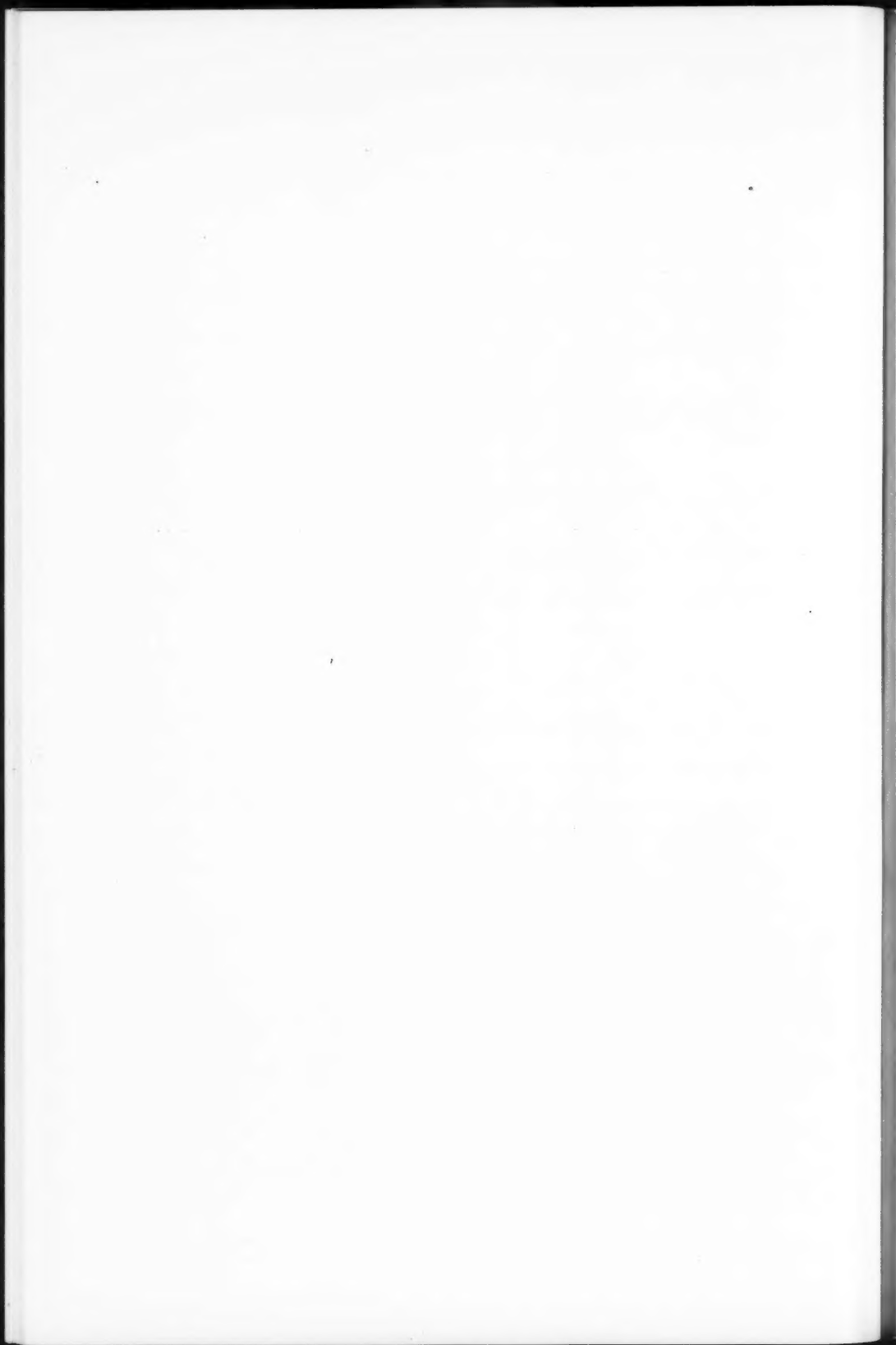
Case II.—H. L., female infant, aged 4½ months, was brought to the Children's Clinic when 7 weeks old on account of being constipated since birth. The child looked unhappy and cried a good deal. An umbilical hernia was present. The cause of the constipation was a tight anus, which was dilated. The bowels have been opened daily since without medicine. This child is also breast fed.

There must be many children suffering similarly, and the cure in this type of constipation is certainly simple and apparently lasting.

Dr. L. S. T. BURRELL showed a case illustrating "The effect of Posture on Intra-thoracic Pressure and the Position of the Viscera."

CORRIGENDUM.

In Dr. PARKES WEBER's remarks in Discussion on Dr. D. C. HARE's "Case of Arthritis with Multiple Subcutaneous Nodules and Sclerodactylia," p. 36, lines 9 and 10 from bottom: "This was the condition of patients with the atrophic and scar-like fingers of advanced sclerodactylia sometimes described as having preceded the cicatricial, advanced stage of the disease,"—for "condition of" read "condition that."



PROCEEDINGS
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UNDER THE DIRECTION OF
THE EDITORIAL COMMITTEE

VOLUME THE NINETEENTH

SESSION 1925-26

SECTION OF COMPARATIVE MEDICINE



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1926

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The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Section of Comparative Medicine.

President—Mr. FREDERICK T. G. HOBDAY, C.M.G., F.R.C.V.S.

President's Address.

By FREDERICK T. G. HOBDAY, C.M.G., F.R.C.V.S., F.R.S.E.

It is customary at the commencement of a Session for the President to say a few words by way of a Presidential Address, but on this occasion, except for an expression of appreciation on my part for the great honour which you have done me by electing me for the second time to the Presidential Chair, I shall say very little. It is indeed a great honour, and one which I appreciate very much, for the Section of Comparative Medicine is a very live one, and can fairly be said now to have got its footing firmly amongst all the other great and important branches which, when combined together, make up the Royal Society of Medicine. It had the advantage at the commencement of being launched under the presidency of a very distinguished and learned scientist—I refer to the late Right Hon. Sir Clifford Allbutt, and it has an advantage over other Sections in that we draw for our membership equally upon the two branches of medicine, the human and the veterinary. Each of these is a life study in itself and each is equally important to the community. For many years they have gone along side by side, but in watertight compartments, and the Royal Society of Medicine can legitimately claim, through its idea of the Comparative Medicine Section, that it has pioneered the way to many new fields of work and thought which might otherwise have been missed. The bringing together under one roof, and at one time, of the workers in the human and animal fields of medicine must necessarily be of mutual help, for the analogies are many, and the diseases, too, are often very similar. Whether they are similar or whether they are different, the study is equally fascinating, and the fact that one animal possesses an immunity to a disease which will with certainty be fatal to another, sets one wondering as to what can be the reason for this. Why, for example, should glanders be so fatal to man and horse, whereas the ox possesses an absolute immunity to it. The diseases, too, which are communicable from animals to man have an especial place for mutual study in a Section of Comparative Medicine. The titles of the papers which have been read during the past two years well illustrate the interest which both branches of medicine have taken in our pioneer effort. There has been no lack of material, and no lack of enthusiasm, and the essayists have been equally drawn from human and veterinary graduates. We have had an average attendance of forty-six, and we are one of the largest numerically, numbering some 197 members. As you know, too, by our rules of constitution our Vice-Presidents and our Members of Council are selected in equal numbers from either branch. The Secretaries too are paired off in this way, and the President alternates after each term of office. Collaboration between the medical and veterinary professions has been much furthered by our Section, and that this is not merely an empty assertion is proved by the fact that all over Great Britain our lead has been followed in the shape of united meetings between branches of the British Medical Association and those of the National Veterinary Association. Socially, too, as well as scientifically, this closer study of Comparative work has brought us into more intimate contact, and in many ways I think that we can legitimately claim to have perceptibly helped forward the mobilization of the forces which are employed in the fight against disease.

2 Andrews: *Recent Advances in our Knowledge of Plant Poisoning*

Dr. Andrews, our first veterinary graduate to obtain the D.Sc. of the University of London, is waiting to give us his paper on "Plant Poisoning," and equally distinguished medical men are here to take part in the discussion; so that you will see that we are commencing our session in the orthodox manner; that is, with the joint collaboration of medical men and a veterinarian. My ambition is to make this session as successful as has been the one which we have just completed, and for this the chief thing necessary is that we shall all bring forward material of mutual interest either in the form of actual specimens or of subjects for discussion.

Some Recent Advances in our Knowledge of Plant Poisoning.

By W. H. ANDREWS, D.Sc., M.R.C.V.S.

It is not proposed here to attempt to review all the recent literature on the subject, but to discuss only certain observations and experiments which appear to be of particular interest and importance. Some of the conditions to be discussed have occurred over wide areas, and have caused serious economic losses, but perhaps their chief importance for us lies rather in the nature of the effects which have been traced to some forms of plant poisoning, the conditions under which those effects are produced, and the further possibilities which are revealed.

It is difficult to form any very definite opinion as to the actual importance of poisonous plants as a cause of losses among the domestic animals in Great Britain. As far as I am aware, there are no statistics relating to this subject, and one has to take into account the very incomplete nature of our knowledge and the difficulties of diagnosis. Long [1] states that there can be little doubt that the financial losses are, in the aggregate, very heavy. Those due to this cause are undoubtedly much greater in some of the younger countries overseas; the reason for this lies mainly in the fact that the animals in those countries graze to a considerable extent over natural mixed vegetation, but in some regions the not uncommon occurrence of drought is an important factor.

These intoxications occur with the greatest severity in areas in which the farms have recently been much reduced in size, as can be seen in some parts of South Africa. The limitation of the grazing area imposes new restrictions on the animals' choice of diet, before any compensatory changes in the grazing can be effected, and the losses from this cause must be expected to increase during the period of transition from extensive ranching to intensive farming.

It is possible, however, that the difference between the younger countries and Britain, in this respect, is not really so great as it appears to be. Where the farms are much larger, it naturally happens that the individual owner has usually a much larger number of animals exposed to the same general conditions; consequently heavier losses fall on individuals, and an owner's grief or resentment appears to be proportional to his absolute, rather than his percentage, loss. Such losses are therefore more likely to be reported. Moreover, each veterinarian works over a very much wider area, and, as there is usually no other veterinarian at hand, he receives all the reports, and is soon aware of the occurrence of any serious condition.

There have been instances of losses caused by the introduction and subsequent spread of a plant from another country, e.g., the case of *Passiflora alba* [2] in Queensland. The risk of such importations into this country may not be at all great, but we have to bear in mind the increasing extent to which our animals are fed on imported foodstuffs, and the danger that poisonous plants alien to this country may reach them by this channel.

The present state of our knowledge of poisonous plants is by no means satisfactory. Fairly complete investigations, including the necessary chemical and pharmacological studies, have been made of a number of plants that contain active principles which are, or have been, used in therapeutics; also of some that have been used extensively, as foods, and of a few that have attracted attention on account of the severity of the losses induced, or the peculiar nature of the effects. But even in connexion with many of these there are many gaps in our knowledge. In a recent paper Craig and Kehoe [3] pointed out the necessity for more detailed work in connexion with such common substances as potato and linseed.

When we pass from the classes of plants already mentioned, however, we soon pass into regions of speculation and assumption. One has no hesitation in asserting that a very considerable proportion of the plants believed to be poisonous, and mentioned in books on the subject, have never been proved to be so; and I consider it to be very probable that definite tests would clear many of them of all suspicion, while experiment would probably incriminate some others which have never been suspected at all.

Even chemical analyses, not preceded by and based on biological experiment, may be misleading from the toxicological point of view; there are some plants which undoubtedly have poisonous constituents, and yet are most unlikely ever to kill animals, and they may even be incapable under natural conditions of doing so. This certainly applies to some plants which have been shown to contain cyanogenetic glucosides, and to some that contain oxalate, e.g., the sorrel investigated by Craig and Kehoe [4]. The active principle may be present in such low concentration that an effective dose is never taken, unless there is cumulative action; this is particularly likely to be the case when the plant is unattractive to animals, and a plant may be so unpalatable that it is rejected after several days of starvation.

In most of the publications on poisonous plants, reference is made to the absence, in many cases, of any really definite evidence, and it is suggested that some of the recorded suspicions are probably not well-founded.

Ewart [5], writing of the poisonous plants of Victoria, remarked that in suspected cases of poisoning, and in the absence of any known poison, it is common to select as a scapegoat one of the plants growing in the vicinity. This plant then acquires a certain reputation which is likely to increase, since the plant is afterwards looked for in other obscure outbreaks, and may quite probably be found in the vicinity. There may, therefore, actually seem to be corroborative evidence, although the first suspicions have been baseless.

Another paper by Craig and Kehoe [4] is of very great interest, as it emphasizes the need for experimental investigation before cases of illness and death are attributed to plant poisoning. In this instance an acute bovine disease was observed to occur in the spring and autumn in a certain district in Ireland, and evidence of the usual kind led to the suspicion that the disease was associated with the ingestion of a common plant, *Rumex acetosa*, or sorrel, which had already been under suspicion in connexion with outbreaks occurring elsewhere. Moreover, chemical analysis confirmed the previously recorded fact that sorrel, like some other species of *Rumex*, contained oxalate. But in this instance actual feeding-tests were carried out on cattle, and the results were negative in all cases, although one animal ate as much as 269 lb. of the plant.

There are many other sources of error connected with a knowledge based on field observations with so small a proportion of critical experimental work. Even when a certain plant or plant-product has been fed to animals and consumed in known amount, and when certain ill-effects can quite definitely be associated with that feeding, there still remain a number of questions which require careful consideration, but which have not by any means always received it.

One of these is the state of the material, i.e., whether it has undergone any

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fermentative or other changes as a result of either parasitic invasion or the action of enzymes pre-existing in the plant, and one must recognize the possibility that parasites may flourish on vegetation and form toxic metabolites without inducing any macroscopic changes in the plants.

Still another very important question is that of the purity of the material or its possible contamination with some other plant species, as in the case of a weed growing amidst a cultivated crop. That a most important error may have arisen from this cause is suggested by the very interesting results obtained recently by Anderson, Howard, and Simonsen [6] in their work on lathyrism.

In man lathyrism probably ranks next to ergotism as the commonest, or, at least, the best known, form of chronic poisoning by vegetable food; it has been recorded on numerous occasions in horses and less frequently in cattle, sheep, and pigs.

The condition of lathyrism has long been known to be associated with the continued ingestion of the grain or seeds of various species of *Lathyrus*, known as dog-tooth, Indian or mutter peas, but attempts to isolate the active principle have given conflicting and inconclusive results. The evidence furnished by the study of naturally occurring outbreaks and by a few feeding tests has been rather unsatisfactory, and difficult to interpret; it has suggested at least that there may be some striking differences in toxicity between various samples of the grain. In their recent work Anderson, Howard, and Simonsen found that *Lathyrus* seeds have no harmful effects on animals, but that the growing crops of *Lathyrus* are always contaminated with leguminous weeds, of which the seeds in some cases resemble the *Lathyrus* grain in appearance. They claim to have associated the condition of lathyrism with the occurrence of the seeds of one of these weeds, *Vicia sativa*, a vetch known as atka, and in the seeds in question they found a glucoside, *vicin*, which on hydrolysis yielded a base, *divicine*, a pyrimidine derivative to which they attribute the ill-effects. The conflicting evidence relating to lathyrism is easily understood if we accept the conclusions of these workers, and their results, if confirmed, will advance our knowledge very considerably. In any case the error that they claim to have detected is of a kind that may have arisen in connexion with conditions other than lathyrism.

Another possible cause of confusion, that may explain some of the cases in which the evidence seems to be contradictory, is the occurrence within a given botanical species of several well-differentiated varieties, which may differ chemically; in this connexion, perhaps, quantitative differences are especially likely to occur. Many of these varieties are, of course, well recognized; others have probably not yet received attention, and it is possible that re-examination of some of the varieties would lead to their recognition as distinct species.

I have been informed by botanical friends of the occurrence of considerable varietal differences within the species *Ricinus communis*, and in some of the species of *Senecio*, and it is of interest to note that in both of these instances there is some evidence of rather wide differences in toxicity. For example, cases have been recorded in which serious effects have been induced in man by the ingestion of one or two castor beans; yet in certain areas children often consume quite a number of the beans without suffering any noticeable harm. It is admitted, of course, that such variations in toxicity may be associated with climatic and telluric, rather than botanical, differences.

It may appear strange, in considering the recent advances in our knowledge of plant-poisoning, that one should discuss at length the value of our present knowledge, and certain causes of error which have probably been in operation. I believe, however, that the realization of the true value of much that has been accepted as fact, and of the urgent need for more detailed and controlled experimental study, in itself constitutes a most important and necessary advance. Those recent investigations that have emphasized this aspect appear to possess, on that account, an added importance.

It would be a very grave error to under-estimate the value of field observations; such observations call attention to the problems encountered in everyday practice, and they necessarily precede and stimulate experimental investigation. Moreover, there are some aspects of the subject which can be studied only in the field, under natural conditions, and it is most desirable that practitioners should record, with the greatest possible detail, the outbreaks of poisoning, or supposed poisoning, which come to their notice. Such records will have a greater value, however, when we are careful to recognize the essential difference between field observations and suitably arranged and controlled experiments, which could not possibly be carried out under the ordinary conditions of practice.

Of the many factors which may affect the toxicity of plants of a given species, one that is well recognized to be important is the character of the soil in which they grow. An excellent example of the influence of soil is afforded by *Vangueria pygmaea* [7], which was shown by Theiler to be more toxic when grown on a certain red soil than when occurring on a black soil found on the same farm; here the altitude and general climatic conditions were more or less identical.

Seasonal variations in plant-poisoning are sometimes due to the fact that a particular plant is found in abundance only at some special, and possibly quite brief, season of the year. In many cases the importance of the season lies, not so much in its influence on the poisonous plant itself, but rather in its effect on the growth of other plants which offer a harmless alternative diet. The spring is naturally the season during which this factor is of the greatest importance, and probably a considerable proportion of the poisonous plants are rarely eaten, in any significant amount, if such an alternative diet is available. The importance of this factor has been demonstrated in connexion with a number of the forms of poisoning investigated recently.

In some cases, however, the toxicity varies greatly at different stages of the plant's growth. Thus Theiler found that *Tribulus terrestris* is poisonous only when in the flowering stage, and one of my former colleagues at Pretoria has shown some striking differences to exist between leaves of various ages on the "gift-blaar" (not yet published). The case of trefoil dermatitis [8] is interesting, since its occurrence at a particular season has been shown by Dodd to be due to the fact that at that time shearing is carried out, and the sensitized skin is exposed to direct sunlight.

The kind of season, or the weather, acts chiefly through its influence on the quantitative relations between the different constituents of the vegetation, as in the case of *Matricaria nigellifolia* [9]. Sometimes the effect is a more direct one, however, and *Tribulus terrestris* [10] seems to lose its toxicity rapidly when dry weather causes a withering or drying of the leaves.

An example of poisoning due to the invasion of a plant by a parasite is furnished by the infection of the grass, *Paspalum dilatatum*, by a fungus, *Claviceps paspali* [11]: this has been shown by Mitchell to induce in cattle an intoxication with nervous symptoms. In this connexion it is interesting to note the observation of Theiler, that *Tribulus* infected with a common fungus appears to lose its toxicity for sheep. Dodd mentions that it is commonly held in Australia that trefoil induces the dermatitis only when the plants are infested with aphides; in fact, "aphis disease" is a popular name for the condition. He reproduced the disease by feeding on trefoil which apparently was free from aphides, but it is interesting to learn that the same idea has arisen in Upper Egypt [12].

Of the changes that may occur in dead plant material, the most important is probably the development in it of the toxin of *Bacillus botulinus*. A great deal of work has been done of late on this subject, and a point which deserves to be emphasized is that there may be no gross changes in vegetable material that is dangerously infected. Mitchell has investigated an intoxication in bovines, with nervous symptoms, and has traced it to the ingestion of maize (chiefly old cobs lying on the ground) infested with a fungus, *Diplodia zeae* [13].

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An article published in 1921 by Zschokke [14] draws attention to obscure but sometimes serious outbreaks of poisoning associated with the ingestion of new or "sweated" hay; he emphasizes the lack of definite information, and the need for further work.

The most extraordinary observations of this kind, however, are probably those recorded by Stockman in connexion with the meal of the soya bean [15]. It appears that no harm whatever is sustained from the ingestion of untreated soya beans, or by animals which consume soya meal from which the oil has been extracted with naphtha. Yet the most striking and fatal effects are induced in cows when the oil has been extracted with trichlorethylene. The trichlorethylene itself is not directly responsible for the intoxication, which cannot at present be explained, and the case is of such interest that further work on it is desirable.

Of recent attempts to isolate the active principles of plants, the most important is probably that already mentioned in connexion with lathyrism. Lathyrism is one of those conditions which may be associated with a latent period, i.e., an interval of considerable length may elapse between the consumption of the poison and the appearance of the first symptoms. The active principles have hitherto been isolated from only one member of this group, *Senecio latifolius*, in which two alkaloids occur; one of these was found by Cushny to have effects similar to those induced by the whole plant.

The work with *Adenia digitata* [16] is worthy of mention; in the first place, a new member has been added to the small list of phytotoxins or toxalbumins; secondly, the phytotoxin "modeccin" resembles ricin in its extraordinarily high degree of toxicity, and in its general effects, but differs in that it does not cause hæmagglutination. Moreover the plant contains two poisonous principles of such widely different classes as a cyanogenetic glucoside (along with an appropriate enzyme) and the phytotoxin. It may be noted here that this phytotoxin has caused fatal poisoning in man.

In considering the effects of poisons on animals, one aspect of great interest is the different character of the reactions that may be shown by various animal species. Examples of such differences have long been known in connexion with such drugs as opium, but recent work with poisonous plants has furnished further evidence of this kind. For example, several species of *Senecio* induce in horses hepatic changes which end in a progressive cirrhosis, and the symptoms, which at first point to hepatic and general digestive disturbance, are later mainly of a nervous character. In cattle a cirrhosis of the liver occurs, but the clinical symptoms may be chiefly connected with the intestine, persistent straining being a prominent and very characteristic sign.

In the case of a *Crotalaria*, the main effect in horses is to be found in the lungs, and the pulmonary symptoms predominate; in cattle the effects are quite different, as pulmonary lesions are absent. In these cases one has to remember the possibility that more than one active principle may be present.

Still more striking are cases in which only one species of (domestic) animal is susceptible. For example, with *Matricaria nigellæfolia* [9] an intoxication could be induced in cattle by giving as little as 21 lb. of the plant, but no ill-effects were seen in animals of any other species, although they were given relatively very much larger quantities (horses up to 235 lb.; sheep 27½ lb.; goat 18 lb.; pig 48 lb.; also a dog, rabbits and guinea-pigs). Similarly the soya intoxication was recorded by Stockman only in bovines, and experimental feeding of sheep and pigs failed to reproduce the condition.

There are other instances of plant poisonings which occur naturally in one species only, but in some of these cases the species which is harmed by the plant may be the only one to eat it in significant amount.

Considerable differences may be noted among animals of one species, and in a

number of instances (such as that of soya) bovine intoxications affect milch cows largely, and even almost exclusively, although an exception to this rule is recorded by Dodd in the case of *Passiflora alba*. Heavy and almost continuous lactation, along with repeated pregnancies, should naturally cause the milch cow to require more food, but the appetite is often not merely greater; it is actually abnormal or depraved, and milch cows generally show some loss of discrimination.

It must be admitted that it is not easy to define the term "poison" in a satisfactory manner, and it is equally difficult to decide whether certain disturbances of health should properly be considered as cases of poisoning. Between obvious cases of poisoning on the one hand, and cases of ill-health due to the unsuitable nature of the diet on the other, there are borderline cases which are difficult to classify.

Although we may confine our attention strictly to conditions which must be classed as poisonings, we cannot, however, fail to be struck by the great variety of the clinical symptoms and post-mortem lesions which may be encountered.

Certain forms of poisoning are often spoken of as "typical," and such terms are usually applied to conditions set up by the action of some irritant. The frequency with which irritant poisoning occurs, and the large number of agents which act (at least mainly) as irritants, provide some justification for the view that such effects as acute gastro-enteritis are fairly characteristic of poisoning. In quite a number of instances, however, poisons cannot be classed as irritants, narcotics, or narcoto-irritants, and much of the recent work has emphasized the facts that the symptoms and lesions of poisoning may be of many different types, and that almost any symptom might prove to be associated with a plant intoxication.

For example, until recently one would hardly have regarded fever as a symptom of poisoning; observations had indicated that raised temperatures might be encountered in some forms, but the occurrence of a high and prolonged temperature reaction would have been considered to suggest very strongly that the condition under observation was caused by a micro-organism. Yet fever is a constant and characteristic feature of the intoxications due to bracken [17], soya meal, *Tribulus terrestris*, and *Crotalaria dura* [18].

Stockman has drawn attention to the similarity of the lesions of acute scurvy to those seen in the intoxications set up by bracken and soya; here the numerous and often extensive hæmorrhages seem to indicate some lesion of the walls of the blood-vessels.

Hepatitis and cirrhosis of the liver occur in a considerable number of chronic plant intoxications, such as those due to various species of *Senecio*, and to *Tribulus terrestris*, and *Crotalaria dura*; in most of these cases the earlier symptoms are associated especially with the alimentary tract, but in the advanced stages severe nervous symptoms may develop very suddenly.

Vangueria pygmaea has been shown to be the cause of "gouwziekte" in sheep, and, as indicated by the name ("quick disease"), the disease is usually of very short duration, death occurring suddenly from heart-failure. In this intoxication the main lesion is a myocarditis, associated with dilatation of the ventricles.

Perhaps the most striking instance of the occurrence of effects that previously would never have been associated with an intoxication, is found in the South African "jagziekte," a condition in horses induced by the ingestion of *Crotalaria dura*. This condition is characterized during life by fever and severe pulmonary symptoms, and post-mortem one finds a form of chronic pneumonia.

A very interesting form of intoxication is one in which the skin undergoes some process of sensitization, and reacts excessively to the action of direct sunlight. This sensitization, or at least the visible proof of it, may be limited to a special region, e.g., in tribulosis it is confined to the head. In a considerable number of other instances the whole of the surface appears to be sensitized, although visible effects, in the form of a localized dermatitis, occur only where the action of sunlight is permitted by the

absence of pigment, and of an excessive covering of hair or wool. In this connexion one may draw attention to the experiments of Dodd in Australia with trefoil and *Hypericum perforatum* [19]. Similar conditions are known to be induced by several plants, in addition to those already mentioned, e.g., buckwheat, several species of clover, and lucerne, and other leguminous plants are suspected. Such conditions have evidently a wide distribution, and a disease of this kind is mentioned in the report for 1924 of the veterinary service of the Dutch East Indies. Very recently Harvey [20] has reported a similar condition affecting young horses in Cornwall.

It is to be noted that most of what we may regard as the strange or unusual forms of plant poisoning appear only after repeated or long-continued ingestion of the plant, and in most of them a period of latency has been shown to occur.

In 1912, Lander [21], referring chiefly to mineral poisoning, stated that chronic poisoning is not common in animals. Chronic poisoning in man is particularly associated with certain special occupations, and the domestic animals are not very commonly exposed to similar conditions. Chronic poisoning by plants, however, is now recognized to be by no means uncommon, and to cause serious economic losses. Some forms have been known, or partially known, for a long time, although they appear to have received less attention than they deserved, but recent work has tended very much to emphasize their importance. In some countries overseas many of the most serious animal diseases have been shown to be of this nature, and in this country Stockman has published observations on a number of such conditions—ragwort, bracken and soya poisoning.

Experiments have demonstrated the necessity of feeding comparatively very large quantities of certain plants, in order to induce intoxication. Such large amounts as are required in most of these cases could not be consumed within a very short period, and in many instances animals would refuse to eat more than a limited quantity at any time, so that the feeding necessarily occupies some considerable number of days.

In some instances the delay in the appearance of symptoms may be due mainly to the fact that the active principle is present in the plant in very low concentration, but that it is only slowly excreted, and accumulates when small amounts are repeatedly taken. In all cases such an accumulation may perhaps be a necessary part of the process leading to an intoxication, but in a number of instances more than this is involved, and it is clear that the effects will develop only after a certain interval of time, whatever the amount fed. In fact, if an animal can be induced to eat a sufficient amount within a fairly short time, there will be a long interval, after the cessation of such feeding, before the effects appear, and there is revealed a latent period comparable to the incubation period of a microbial disease. Sometimes one can obtain indications as to the possible length of the period, from a study of the circumstances associated with natural outbreaks; in this way it has been estimated that with bracken the period may be at least two weeks, and with *Senecio jacobaea* [22] at least three weeks.

The following periods have been recorded under experimental conditions: Soya meal, twenty-eight days; *Vangueria pygmaea*, thirty-seven days; *Matricaria nigellifolia*, forty-two days; *Crotalaria dura*, eighty days; and *Senecio latifolius* [23] ninety-six days.

It should be recognized that the latent periods given in the above list are the maximum periods which have been recorded, but that it is quite possible that under different conditions these periods might be exceeded. In experiments with *Matricaria*, it was observed that after eating, during the course of five days, an amount bordering on the minimum lethal dose, an animal developed symptoms after a latent period of forty-two days, i.e., on the forty-seventh day from the commencement of feeding. The consumption of seven or eight times that amount only reduced the time to twenty-three days, and giving what was probably nearly 20 minimum lethal doses (in the more concentrated form of hay) only reduced the period to twenty days.

There are records of latent periods occurring in lathyrism—up to twenty-two days in cattle and even fifty-four days in horses; *Lathyrus* is said to take on an average about four months to induce visible effects in man, but there do not appear to be any recorded observations that would permit one to conclude that in man also a latent period may be seen, although its possible occurrence may be assumed. It may be added that another intoxication of this group, *Senecio* poisoning, may probably occur in man; certain human cases of liver cirrhosis in South Africa have been ascribed by Willmott and Robertson [24] to the action of seeds of *S. latifolius* and *S. Burchelli*, which may occur amongst wheat.

It may be noted that in some of the investigations into these chronic intoxications particular care has been taken to exclude bacteria and their products, by feeding sterilized material; for example, cases of *Matricaria* intoxication were induced by feeding material which had been autoclaved for twenty minutes at 115° C.

In connexion with his bracken experiments, and in view of the resemblance to acute scurvy, Stockman took special pains to exclude any possibility of inducing an avitaminosis, and in most experiments of this kind the total diet has not been such as to suggest that possibility. Moreover, as shown by Theiler, Green and Viljoen [25], it seems to be exceedingly difficult to induce, in most of the domestic animals, anything of the nature of a specific avitaminosis.

In many of these conditions, the effects appear with quite explosive suddenness. In the case of one animal fed on *Matricaria* for ten days, and then left to graze in a field known to be free from the plant, the first symptoms appeared twenty-five days after the beginning of the feeding, and fifteen days after its termination. On the twenty-first day, eleven days after the last *Matricaria* feed, the writer had occasion to watch the experimental animals being put through a dipping tank (an arsenical dip used to eradicate ticks), and the animal in question was particularly noted to give considerable trouble on account of its strength and agility. These observations proved of special interest four days later, when symptoms developed; and also on the following day, when the animal was quite unable to stand, and appeared to be unconscious of its surroundings.

In some of these conditions, such as *Senecio* intoxication, the changes in the liver suggest that there may be retention and accumulation of the toxic substance in the liver, with subsequent necrosis of hepatic cells and liberation of the poison. In crotalaria, the pulmonary lesions may possibly be due to excretion of the active principle (at present unknown) by the lung. But in a number of these intoxications there is no well-defined lesion, such as a cirrhosis of the liver.

The occurrence of these latent periods is of great interest, and may perhaps throw some light on chronic poisoning in general. The usual view is that symptoms of chronic poisoning are delayed until the excess of absorption over excretion (and destruction) causes the concentration to reach a certain level, i.e., there is accumulation of substance. But in these latent cases no more accumulation can possibly be occurring, and the symptoms obviously appear when a certain degree of injury has been sustained. Although there may at first be some accumulation, there is undoubtedly summation of effect, and some progressive form of injury; it must be admitted that the changes occurring in the body, during the latent period, may lead to the raising of the concentration of the poison in some particular region. It may be that the time factor is of importance in this connexion, i.e., that injury to certain tissues may be induced more easily by prolonged exposure to a certain concentration, than by short exposure to a much higher concentration of the poison. In experiments with *Matricaria* there was some evidence suggesting that a smaller dose may become effective if its administration be spread over a longer period; but it was not conclusive, and further work is needed.

As far as I am aware, no evidence of the existence of a latent period has been recorded in connexion with any of the chronic mineral poisonings of man; probably

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it is not often that susceptible individuals, exposed to risk of chronic poisoning through following some special occupation, change entirely to another environment before symptoms develop.

The very important features of these latent intoxications are: (1) The probability of their not being recognized as plant poisonings at all. (2) The difficulty of finding the cause, even when its nature is suspected. If the plant in question has been eaten weeks, and even months, previously, at the time of the appearance of the first symptoms the animals may have been moved to pasture which is quite free from it. Even when no such movement has taken place, seasonal changes may have caused the plant to become very scarce, and even to disappear entirely.

The conditions under which animals are tempted to eat poisonous plants are of considerable importance. We have still much to learn on this subject, and the greater part of the necessary information can be collected and recorded only by workers in the field. Excessive hunger is doubtless the main cause of the consumption of poisonous plants, and that arises from a relative scarcity of other foodstuffs, which is due most commonly to particular weather conditions, drought especially. Placing too many animals on a given grazing area will obviously have the same effect of inducing a shortage of other and more palatable foodstuffs. Animals which have been travelling are particularly liable to eat poisonous plants; probably this is often merely a matter of hunger.

An interesting point is the difference which is often observed between the animals bred in one particular area, and those which have recently been introduced to it. The usual explanation of the avoidance of poisonous plants by native animals is that their consumption on some previous occasion has been followed by unpleasant, although not necessarily serious, effects. This explanation cannot hold good for chronic intoxications, for no animal could associate pain with something eaten weeks or months previously; but it was observed that native cattle sometimes escaped *Matricaria* poisoning, although imported animals kept on the same pasture suffered severely. When animals which had recovered from the intoxication were tested, they showed no special dislike for the plant, but actually took it more readily than most of the newcomers. There is reason to suppose that in some of these cases a degree of tolerance is established.

I believe that the most probable explanation of the difference in behaviour between native and newly-introduced animals, is that the former have learned to know the local vegetation, and to discriminate between plants of varying grades of palatability; whereas the newcomer, apart from the fact that it may be excessively hungry on its arrival, is introduced to an unfamiliar flora, and has lost its usual bearings; in such a case it is not surprising if the animal is willing to feed on a plant that normally is moderately unpalatable. Craig and Kehoe found that sorrel was eaten very much more readily by cattle that had been stabled for a considerable time, but its rejection by animals taken fresh from pasture could hardly be ascribed to memory of past injuries, since feeding-tests indicated that no injuries are inflicted.

The development of a habit, or an actual craving for a certain poisonous plant, appears to be very rare, although it is described in connexion with loco weeds. I observed in one case signs of what seemed to be a craving for the usually unattractive *Matricaria nigellæfolia*, but further examination showed that the condition was really one of almost total loss of the ordinary ability to discriminate.

In considering the causes of poisoning in bovines, it is well to bear in mind the fact that these animals appear to be particularly liable to suffer from depraved appetite, as has been shown by the publications of Theiler and his co-workers on osteophagia and phosphorus deficiency.

With respect to methods of prevention, the most obvious course is to eradicate an offending plant, and in some cases that could, and most certainly should, be done. In many cases it would be a slow, difficult and costly operation, and one that might

not be justifiable economically. In some instances one would have to regard eradication as practically impossible, at least for the present, and in certain cases it might even be undesirable. It should not be forgotten that some of the poisonous plants are eaten by animals, only when climatic or other conditions have interfered with the growth of the ordinary pasture plants, with the result that poisonous plants predominate in the vegetation. This quality of being able to withstand adverse conditions may be of great value, and the nutritive value of such plants (apart from toxic effects) may be fairly high; moreover, the plant in some instances is harmless to several of the species of domestic animals.

Where eradication is difficult or impossible, by careful study of the intoxication we may be able to devise means of preventing it. In some instances we can obviously utilize the plant as food for animals of species which are not susceptible to the intoxication, but even a susceptible species may be efficiently protected by some simple precaution adapted to the particular case. In some cases (as with *Tribulus*) it would be sufficient if one insured a proper dilution of the material, by giving an adequate quantity of other foodstuffs.

In other cases all ill-effects might be avoided by making the feeding discontinuous; it would not be difficult to ascertain experimentally what intervals had to be observed, and it might well prove that one could safely allow animals to graze in the danger zone on two or three days a week. Such a method might enable a stock-owner to pass through a period of drought and shortage with comparatively negligible losses, whereas the complete loss of the use of the particular pasture might lead to disastrous consequences. It is also quite probable that research would enable us in some instances to devise a practical method of rendering animals tolerant.

In conclusion, it may be claimed that the additions to our knowledge of plant poisoning during the past decade have been of considerable importance, and of great interest. They have undoubtedly added much to our store of useful knowledge, but they have also emphasized the need for more and wider research.

In investigations of this subject it is most desirable that the first work should be biological. It is clearly a waste of labour, from the toxicological point of view, to devote energy and time to the study of a plant that may not be poisonous at all, and the first step should be to determine whether the plant will cause harm when ingested by animals, and whether any animal is likely ever to consume an effective quantity under any combination of natural conditions. After the performance of suitable biological experiments, the chemist has a reasonable basis for his work; the plant is known definitely to induce certain effects, which can be described more accurately than is possible from observation of natural cases, and the determination of the action on ordinary laboratory animals enables the chemical separations to be checked at each step.

Finally, the later and extremely important work of the pharmacologist will be performed on a substance of known importance, and the preliminary pharmacological studies will be simplified and helped by the possession of a knowledge of the general effects under various conditions and in several different animal species.

REFERENCES.

- [1] LONG, "Plants Poisonous to Live Stock," Cambridge, 1917. [2] DODD, *Journ. Comp. Path.*, 1910, xxiii, p. 205. [3] CRAIG and KEHOE, *Vet. Record*, Sept. 19, 1925, p. 795. [4] *Idem*, *Journ. Comp. Path.*, 1921, xxiv, p. 27. [5] EWART, Quoted by Brenchley, "Weeds of Farm Land," London, 1920. [6] ANDERSON, HOWARD and SIMONSEN, *Ind. Journ. Med. Res.* Abstract in *Lancet*, Sept. 19, 1925. [7] THEILER, Du TOIT and MITCHELL, "Gouwsiekte in Sheep," *Ninth and Tenth Reports of Dir. Vet. Res.*, Pretoria. [8] DODD, *Journ. Comp. Path.*, 1916, xxix, p. 247. [9] ANDREWS, *ibid.*, Dec., 1921, and *Ninth and Tenth Rep. D. V. R.*, Pretoria. [10] THEILER, "Geeldikkop in Sheep," *Seventh and Eighth Rep. D. V. R.*, Pretoria. [11] MITCHELL, *ibid.* [12] RABAGLIATI, *Vet. Record*, Sept. 19, 1925, p. 823. [13] MITCHELL, *Seventh and Eighth Rep. D. V. R.*, Pretoria. [14] ZSCHOKKE, *Sch. Arch. f. Tierheilk.*, 1921, lxi, p. 373. [15] STOCKMAN, *Journ. Comp. Path.*, 1916, xxix, p. 95. [16] GREEN and ANDREWS, *Ninth and Tenth Rep. D. V. R.*, Pretoria. [17] STOCKMAN, *Journ. Comp. Path.*, 1917, xxx, p. 311, and 1922, xxxv, p. 373. [18] THEILER, *Seventh and Eighth Rep. D. V. R.*, Pretoria. [19] DODD, *Journ. Comp. Path.*, 1920, xxxiii, p. 105. [20] HARVEY, *Vet. Record*, Sept. 19, 1925. [21] LANDER, "Veterinary Toxicology," London, 1912. [22] STOCKMAN, *Journ. Comp. Path.*, 1917, xxx, p. 131. [23] THEILER, *Fifth and Sixth Rep. D. V. R.*, Pretoria. [24] WILLMOTT and ROBERTSON, *Lancet*, Oct. 23, 1920. [25] THEILER, GREEN and VILJOEN, *Third and Fourth Rep. D. V. R.*, Pretoria.

12 Andrews: *Recent Advances in our Knowledge of Plant Poisoning*

Discussion.—Dr. MANSON-BAHR alluded to the benefits which had already accrued, and were likely to accrue, from a closer association of the veterinary and medical sciences, and for this reason he congratulated Dr. Andrews on the comprehensive nature of his address: it had given him (the speaker), cause for serious reflection. Dr. Andrews had referred to cirrhosis of the liver in sheep as a sequel to prolonged ingestion of plants belonging to the genus *Senecio*. He drew attention to a peculiar cirrhosis of the liver which occurred amongst adults in India, especially amongst Mohammedans who were abstainers from alcohol. The origin of this disease had so far defied all investigations, whilst a similar cirrhosis appeared to be found in other parts of the tropics amongst the negro tribes of Central Africa to which Dr. Andrews had referred. Might not this disease in man be due to the continued ingestion of some plant poison which, like lead, was cumulative in its effects? A similar cirrhosis of the liver occurred in infants in India, known as "infantile biliary cirrhosis," which appeared to be confined to the Hindu section of the community, the infective virus of which was carried in the mother's milk and was the cause of the occurrence of several cases of this disease in children of the same family.

The lecturer referred to a dermatitis in sheep, due to skin sensitization by the ingestion of toxic proteins brought about when fed upon different forms of clover, trefoil and St. John's wort. The analogy between this condition and the disease known as pellagra in man struck him as being a very close one. All attempts to run to earth the particular virus of pellagra had hitherto failed; it was certainly not a vitamin-deficiency disease. Pellagra was peculiar to certain countries, especially those bordering the Mediterranean, the West Indies and South America. Formerly thought to be due to the ingestion of damaged maize, it was now considered to be in some way connected with the ingestion of some food toxin. The main feature of pellagra was the sensitization of the skin, which caused a peculiar rash to appear wherever it was exposed to the direct rays of the sun. This was proved by the distribution of the rash on the hands and face in early cases of the disease, and also by its artificial production of pigmented patches (such as those caused by holes cut in paper) by a direct light stimulus on different areas of the skin. The prolonged ingestion of the hypothetical pellagra toxin led in time to digestive disturbances and ultimately, by implicating the nervous system, to various pareses, insanity and death. It seemed to him (the speaker) that the ingestion of some mild, but cumulative, plant toxin—some toxic protein—over a long period of time might lead to this skin sensitization and ultimately to involvement of the central nervous system. He (Dr. Manson-Bahr), went so far as to say that the facts brought forward by Dr. Andrews might shed a new light on the ætiology of pellagra—a most important disease—in man, and, ultimately, to a renewed effort disentangling the true ætiology of this mysterious malady.

Dr. J. F. HALLS DALLY said he regarded Dr. Andrews' paper, evidently based on careful and lengthy investigations, as a valuable contribution, not only because of the wealth of facts disclosed, many of which were probably new to Members of the Section, but also on account of the wide and stimulating issues thereby raised. There were four points of special note: (1) The considerable difficulty experienced in assigning the due balance of cause and effect to symptoms manifested by the herds under observation as the result of alleged poisoning by one or other poisonous plant. In certain cases, attribution was necessarily difficult, and likely to be erroneous unless controlled by experienced workers. From the physician's standpoint, he (Dr. Halls Dally) agreed that the *post hoc propter hoc* method of reasoning might lead to the most erroneous deductions, particularly so in the present instance, when one reviewed the extreme variability of the basic factors of seasonal and geographical distribution of plant growth, of climate, of animal migration and acclimatization, &c., in the light of the extraordinarily long latent period so often occurring before onset of the first symptoms. (2) The selective action of plant poisons upon heart, lungs, liver and other organs and tissues; this was entirely in agreement with that exhibited by the toxins of infective processes. He (Dr. Halls Dally) put forward the suggestion that the symptoms in many cases might be due to a specific sensitization. (3) If the author's remarks had been apprehended correctly, he was understood to have claimed that evidences of vitamin deficiency had not been observed in the animals investigated; this was of interest as being at variance with the views put forward at a recent discussion of that Section by Dr. Rowlands, who attributed the immunity of his herds of domestic animals against tuberculosis to careful feeding with balanced vitamins. (4) Dr. Andrews' paper might be regarded as amply supporting the plea so ably made by the President in his opening address for closer co-operation between the medical and veterinary professions, in that this subject of poisoning of domestic animals by plants afforded an extensive field for

investigation in which veterinarians, pharmacologists, biochemists, field workers, and other ancillary groups might alike share.

Dr. F. PARKES WEBER remarked that in investigations concerning cirrhosis of the liver produced by senecios, etc., the various known causes of (experimental) hepatic cirrhosis should be borne in mind, such as colloidal silica, manganese chloride, etc. (W. G. MacCallum thought that protein sensitization might be an important agent in some cases of human cirrhosis of the liver).

[November 25, 1925.]

A Note on the Endocarditis of Swine Erysipelas and its Relation to the Cardiac Infections of Man.

By CAREY F. COOMBS, M.D., F.R.C.P., GEOFFREY HADFIELD, M.D., M.R.C.P., and G. E. HENSON, M.R.C.V.S.

THE inquiry that we are about to describe arose out of the hope that some light might be thrown on the ætiology of cardiac infections in man if such similar lesions as occur in the lower animals were re-examined from the human point of view. A question addressed to the President of this Section resulted in the collection of material by one of us (G. E. H.) which has been examined by us, with results that we shall describe. First, however, we may briefly outline what is generally known about the disease called swine erysipelas and its endocardial complications.

The disease is caused by infection of swine with the *Bacillus rhusiopathiæ suis*, an organism which we do not propose to describe. It is thought to enter the body of its host by way of the alimentary canal. In this country it is more often sporadic than epidemic, though it may assume the characters of an epizootic, as in the Chatteris outbreak of 1905. On the Continent epidemics are frequent.

It is usually a disease of half-grown or adult pigs, and is characterized by high fever, with red or purple patches on the skin, from which the disease gets its name. These are often more or less diamond-shaped, and tend to become confluent, sometimes covering a considerable portion of the body. Internal hæmorrhages are seen on the mucous membranes. The disease usually takes one of two forms. In the first place there is high fever, complete loss of appetite, disinclination to move, discoloration of the skin, appearing after the first or second day, constipation, and frequently a painful swelling of one or more of the neck- and knee-joints, with lameness. These symptoms are followed either by death, usually within forty-eight hours, or by complete recovery within a few days; or the infection may assume a chronic type.

In the second form the primary symptoms are not so marked. The discoloration of the skin is usually but not always present, and not so widespread in its distribution; yet there is the same likelihood of the chronic condition developing.

In this chronic phase the pig regains its appetite and apparently recovers. After a time it develops a persistent cough with quick breathing (especially if it is made to take exercise), a disinclination to move, and visible evidences of cardiac disease. These symptoms become worse, until at the end of two or three months from the onset of the disease the pig dies or is destroyed. Post-mortem examination reveals the presence of cauliflower-like masses on the cardiac valves, usually on those on the left side, but sometimes on both. Occasionally these growths have become so enormous as almost completely to occlude the auriculo-ventricular opening.

It is worthy of note that these masses take an appreciable time to develop, and though their presence may be suspected in a pig with continued unthriftiness following an attack of erysipelas a precise diagnosis is rarely feasible until the pig is extremely ill or, what is more probable, until a post-mortem examination is made.

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Often this is due to the fact that the pig has been only under occasional observation, so that there is no opportunity for watching the evolution of the symptoms.

The history of the pigs from which were taken the specimens examined by us is briefly as follows:—

(1) Two valuable Gloucestershire Old Spot hilt about five months old, belonging to a well-known breeder, were found lying together and disinclined to move. Both had high fever (107° F. to 108° F.), but showed none of the characteristic skin markings. These however, appeared on the following day. The owner was informed of the nature of the disease and of its possible sequelæ. However, when they were next seen about a week later, one had completely recovered, whilst the other showed signs of lameness and swelling in one hock. Ten weeks after the first visit one of us (G. E. H.) was called in again, and found one of them refusing food, almost unable to rise and showing frequent short respirations with cough. There had been considerable deterioration in condition since the first visit. A diagnosis of verrucose endocarditis was offered, and slaughter advised. The heart showed no obvious hypertrophy of its walls nor dilatation of its chambers. The pericardium was glossy and normal. The whole of the endocardium was extensively infected; firmly attached and well-organized thrombi were found on both sides, on all the valves, and on the mural endocardium. The distribution was chiefly left-sided and valvular, the left auriculo-ventricular opening being almost occluded. The vegetations were yellowish-pink and firmly welded to the heart wall; none were softened; all were approximately the same age. This heart was examined microscopically by taking a series of blocks including the musculature of all four chambers and the conducting tissue, and several blocks of the mitral and aortic valves. Even microscopically the lesions proved to be entirely endocardial, the myocardium being only involved superficially where the fibrosis at the base of attachment of a large vegetation had penetrated into it. All the vegetations were well organized and little fibrin remained unabsorbed even in the largest. Their surfaces showed obvious colonization under a thin, superficial layer of necrotic fibrin. The colonies of bacilli were dense and strictly confined to the surface; here and there the depths of the valve were penetrated by a few small bacterial masses, but in no case was the myocardium reached. The greatly increased cellularity of the valve and its extensive vascularization were very striking (see fig. 5, p. 19).

(2) A cross-bred, large white hilt, which was in farrow and due in a week or two, had been ill for several days. Slight red markings were seen and a diagnosis of swine erysipelas was made. The owner stated, a few days later, that it had quite recovered, and had farrowed. When the young pigs were about six weeks old, however, it had to be seen again, as it had become very poor in health and was not feeding. It was found to show signs of heart disease, and as it did not seem likely to live many days, slaughter was advised. The heart was found to show changes similar to those of the first heart, except that the lesions were probably a few weeks older. The vegetations were more deformed by contraction of fibrous tissue, which was more copious, and the number of bacterial masses on their surface was much less.

(3) This pig died suddenly, the owner stating that he had never noticed any signs of ill-health. The heart showed the lesion in an early stage, more suitable for microscopic study. The lesions were small, soft and localized to the aortic and mitral valves. As in the preceding cases, they were all approximately the same age. Photomicrographs of sections of this animal's mitral valve are shown (figs. 3 and 4, pp. 18, 19). We have little doubt from a study of this early case that the endocardial lesions of the disease are due to thrombus-formation over masses of bacteria deposited on the surface of the endocardium out of the blood.

The early vegetations in this case were very heavily colonized and separated from the myocardium only by the relatively little-altered valve, yet the muscle was free from bacilli and inflammatory cells.

(4) Another heart, kindly sent to us by Captain Brand, M.R.C.V.S., showed a stage intermediate between the two more chronic types and the early cases. It was that of a large Yorkshire sow of fifteen months, farrowed nine weeks before death and found dead, not having shown any sign of illness. The vegetations in this case were almost entirely valvular, reddish and easily detached. There was no sign of pericarditis. A thoracic gland from the same animal grew a pure culture of the bacillus. No microscopic examination was made in this case.

(5) Captain Brand also provided us with the heart of a female cross-bred large white, aged 8 months. This animal had been ill fourteen days with interrupted breathing; two others of the same litter had been infected but recovered. This animal had never shown skin lesions.

The bacillus was isolated from the spleen. The heart, which was not examined microscopically, showed subacute endocarditis strictly limited to the mitral valve. The vegetations were very large, fairly easily detached and all of the same age. They almost completely occluded the auriculo-ventricular opening.

The endocardial lesions themselves resemble very closely those seen in the various types of ulcerative endocarditis in man. In the pig the vegetations are larger (figs. 1, 2, pp. 17, 18), show a greater tendency to infect the mural endocardium in the later stage, and the colonization of the surfaces of the valves and endocardium is heavier. In man lesions of this degree and severity are usually accompanied by gross changes in other organs, and the absence of these changes in the pig signifies a considerable degree of general tissue immunity to the infection.

It seems likely that the valvular endocardium is first attacked, as in the early cases the thrombi were almost entirely valvular. That the mural endocardium is infected soon after the valves is probable, as in the chronic stage there was no apparent difference in the degree of organization of the mural and valvular deposits. The striking absence of myocardial and pericardial change found in all the specimens examined confirms the view that the lesions are of the implantation type.

Our main purpose in seeking for knowledge of the cardiac infections of lower animals was to find something that might throw light on the aetiology of cardiac rheumatism in man. The first glance at these hearts of pigs, however, showed that we were dealing with lesions quite different from those of rheumatic carditis as we understand that term. We reserve it for that disease which begins principally in childhood and runs a course of ten to thirty years, punctuated by acute exacerbations which tend to become less frequent as time passes on. The infecting organism is thought to be a streptococcus, the affinities of which are chiefly with those which inhabit the normal alimentary tract of man. The characteristic anatomical change is a carditis, that is, a reaction which is diffused equally and simultaneously through all parts of the cardiac wall, attacking muscle always, valves nearly always, and pericardium more often than not. This general distribution and the relation of the lesions to the blood-vessels in the cardiac wall prove that the infective agent reaches its goal through the coronary arteries, i.e., through the vessels which supply blood to the heart itself. The resultant lesions are productive rather than destructive. The endocardial inflammation begins in the depth of the valves and spreads to the surface, where it produces a uniform fringe of tiny vegetations near the free edge of the cusp. The ultimate change is a thickening and deformity of the valve, which greatly detracts from the mechanical efficiency of the heart.

This is quite a different picture from that of the heart under discussion, which reminded us vividly of two other conditions. The first, that of ulcerative endocarditis in man, rarely attains so gross a degree of change as is seen in the pig heart, yet it is obviously of the same nature. The ulcerative endocarditis of man owes its origin to a variety of organisms; the streptococci, non-haemolytic as well as haemolytic, the pneumococcus and the gonococcus, between them accounting for nearly all cases. As a result of infection of a valve by one or other of these, the endocardial surface becomes necrotic, and on the resulting ulcer fibrin is piled up, masses of organisms colonizing the zone in which valve and fibrin are fused with each other. These masses vary greatly in volume with the nature of the infection; the haemolytic streptococci, for example, grow lavishly, while the non-haemolytic strains may be so scanty that it is impossible to find them, even after cultivation of the vegetations. In all degrees of the disease the endocardial lesions quite overshadow those of the myocardium, which are but occasional and, so to speak, accidental.

Even more like these lesions of swine erysipelas are those seen in the hearts of a certain percentage of rabbits that have been inoculated with non-haemolytic streptococci. In these the vegetations are usually large, sometimes filling up the cardiac

cavities in a way very like that of the lesions of the pig hearts. Microscopical examination bears out this analogy. Both in the erysipelalous endocarditis and in that of the inoculated rabbits two findings are obvious. In the first place, the endocardial lesions are accompanied by widespread and massive implantation and colonization of the infecting organisms in the areas of endothelial necrosis. Secondly, the cardiac muscle is not much damaged; such damage as it does suffer is secondary to that of the endocardium, whence it reaches the muscle either by embolism or by direct extension. In both erysipelalous endocarditis and in the experimental rabbit lesion we may be sure, from this supremacy of the endocardial lesions, and from the way in which bacteria swarm on the endocardial surface (although they are almost absent from the deeper parts of the heart), that the infective agent is implanted on the lining of the cardiac chambers by the circulating blood as it is passing through the heart. The lesions of human ulcerative endocarditis, also, are so similar to those of the two kinds of animal disease that we cannot doubt that they arise in a similar way, i.e., by implantation of the causal bacteria on the endocardial surfaces. (We do not deny that some kinds of human ulcerative endocarditis may prove to be exceptions, but this does not alter the rule.) It may therefore be stated as a general proposition that in the ulcerative endocarditis of man, as well as in the endocarditis of the erysipelalous pig and the inoculated rabbit, the valve is infected from its surface inwards, whilst in rheumatic carditis the endocardial inflammation begins in the depths of the valve and spreads towards the surface.

There are two other features of the endocarditis of swine erysipelas that should interest the student of comparative pathology. First, there is the long period of latency. This is very like what we see in certain types of ulcerative endocarditis in man. Months of vague ill-health may elapse before there is the smallest hint of the presence of an endocardial infection. There may be almost no sign of valvular disease. Yet at autopsy we find, to our surprise, great warty masses clinging to the valves and grossly distorting them. Secondly, it is clear that in the pig, as in the inoculated rabbit, the endocardium is attacked in only a small percentage of the animals into whose general circulation the infecting micro-organisms enter. That this is so in man also is certain. In pneumonia, for example, the pneumococcus gains a hold on the valves in only a small proportion of cases; and again, if we contrast the extent of the area of mucous membranes in the body that are continuously infested with streptococci, with the infrequency of progressive streptococcal endocarditis, we must believe that the valves accept invasion by streptococci in a few only out of the many chances offered to them. There is plenty of evidence to show that successful implantation and colonization of organisms on the surface of the human valve are largely contingent on the existence of certain predisposing conditions of the valve itself, and of the general economy. It would be interesting to know whether analogous conditions are discernible in the pig. For example, are there congenital malformations of the valves similar to those that, in the human subject, are known to lay the endocardium open to infection?

Indeed, the chief purpose of this short exposition has been to collect information rather than to impart it. We want to learn as much as we can about the cardiac infections of the lower animals, and we are grateful to this Section for giving us so excellent an opportunity for making our desires known.

Discussion.—Captain S. R. DOUGLAS said that in the course of examinations of streptococci of various strains he had discovered that the *Streptococcus viridans*, though found in very small numbers in the blood, was very resistant to phagocytosis *in vitro*.

Professor G. H. WOOLDRIDGE observed that outbreaks of swine erysipelas were not so uncommon as was thought at one time. The infection might linger on in animals which had recovered but thus became carriers; for example, a sow might herself recover, yet subsequently infect some of her own litter. He also remarked on the absence of the disease in the United States.

Dr. M. J. ROWLANDS also alluded to the carrier problem, saying that herds might be safeguarded by exposing the weakest member to contact with a suspected carrier.

Dr. H. D. WRIGHT asked whether bacteriemia was present in the late stages of the disease, and whether the animal produced immune bodies.

Dr. PARKES WEBER said he thought that the erysipeloid of Rosenbach might be the human equivalent of swine erysipelas, and asked for information as to the course of lesions in man caused by accidental inoculation from pigs.

Dr. MAX BERG described cases of erysipeloid which had been demonstrated to him by Rosenbach himself.

Mr. R. STOW related a personal experience of what appeared at first to be an inoculation from swine erysipelas.

Mr. A. W. STABLEFORTH, in reply to Dr. Wright, said that in the late stages, bacilli were occasionally present in the blood in small numbers, and could only be detected by making many cultivations; also that antibodies were present in the blood of hyperimmunized pigs, although horses were not always used in producing a protective serum.

Dr. LLOYD JONES asked whether it was true that the myocardium was never attacked; quoting, by way of analogy, the Bracht-Wachter myocardial lesions of endocarditis lenta and of the rabbit inoculated with non-hæmolytic streptococci.

Dr. COOMBS (in reply) said that their view was that in the endocarditis of swine erysipelas as in the ulcerative endocarditis of man, and (for the most part) in the endocarditis of the inoculated rabbit, any myocardial lesions that occurred were secondary to those of the endocardium, the mode of spread being either that of direct continuity or that of embolism.

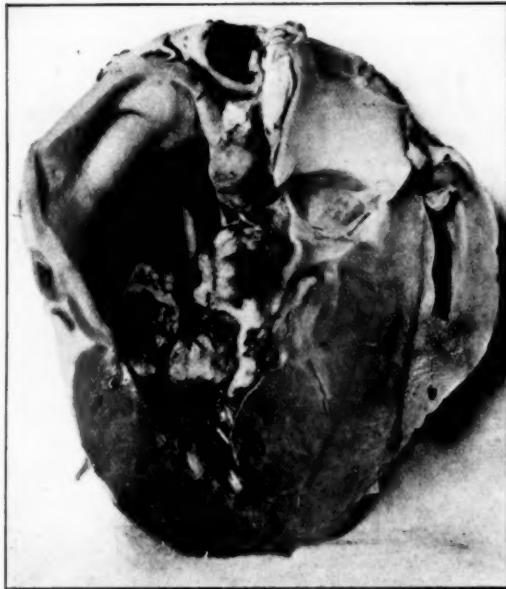


FIG. 1.—The valvular and mural endocarditis occurring in the chronic stage of swine erysipelas.

Large cauliflower-like masses obstruct all the orifices. They are composed of vascularized granulation tissue which is extensively colonized on the surface by the bacillus which causes the bacteriemia.

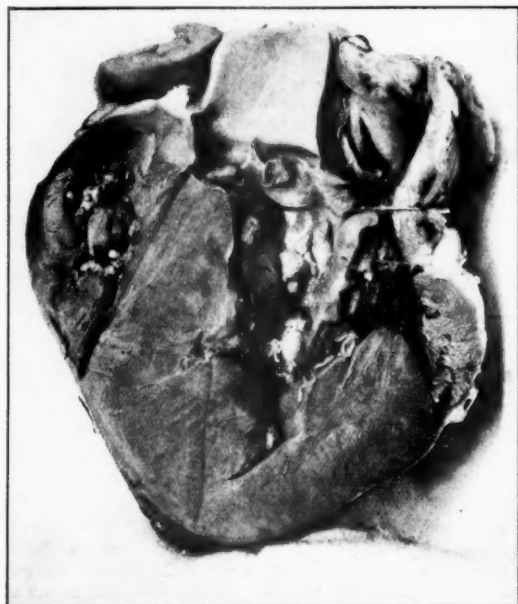


FIG. 2.—Showing the extension of the process of implantation on to the mural endocardium.

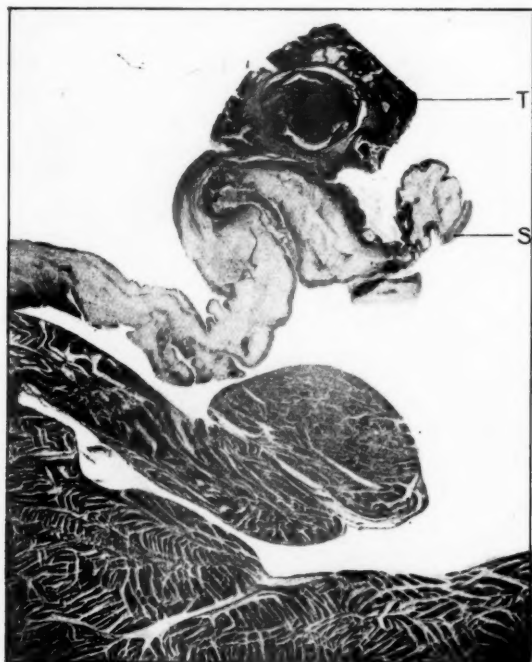


FIG. 3.—Photomicrograph showing the early stage in the evolution of the endocardial lesion.
Mitral valve of a young pig showing a large adherent and heavily-infected thrombus (T) implanted on the surface of the valve. A continuous surface-zone (S), clothing the distal half of the valve, is composed of autolysing fibrin in which large surface colonies of the causative bacilli lie embedded.



FIG. 4.—A high-power view of the mitral valve in the preceding figure. The vegetation is composed of softened autolysing fibrin (F), and its surface heavily plastered with dense bacterial masses. It is attached below by a broad stalk (S) to the valve (V). The surface-zone (SZ) of the valve is extensively colonized.

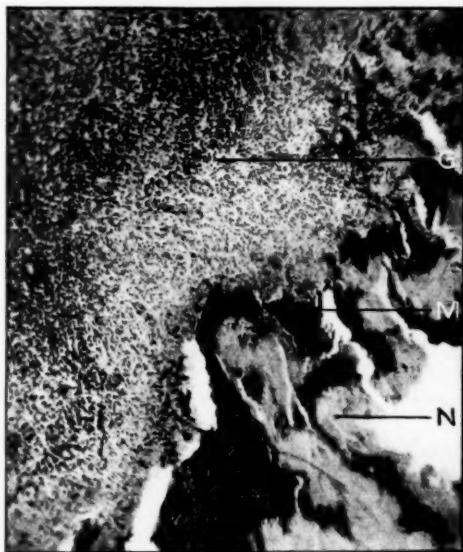
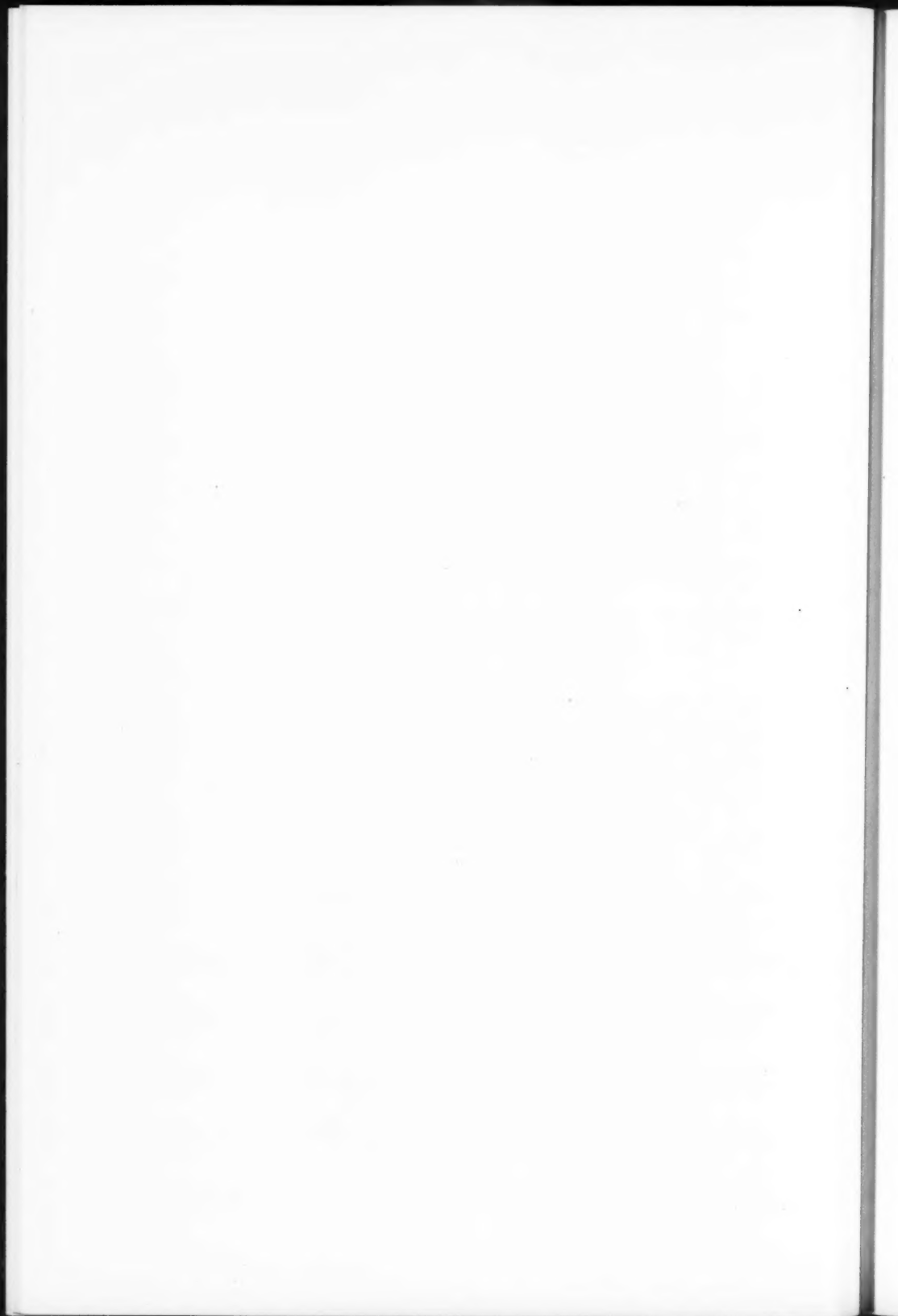


FIG. 5.—Surface of the mitral valve showing surface colonization. The cellularity of the valve is enormously increased and it is vascularized to its edge, i.e., is converted into granulation tissue (G). A surface-layer of neurotic fibrin is seen at (N), and the continuous zone of colonization at (M).



Section of Comparative Medicine.

President—Mr. FREDERICK T. G. HOBDAY, C.M.G., F.R.C.V.S.

The Relation of Quantity of Vitamin B to the Quantity of Food.

By R. H. A. PLIMMER, D.Sc.

A DIET consisting of white rice does not contain vitamin B, and it leads, as is well known, in three to four months to beri-beri in man, and in three to four weeks to polyneuritis in pigeons. It is not so well known, however, that birds and man on large amounts of white rice suffer sooner than those on small amounts, and that climatic conditions as well as exercise have a distinct effect: cold and wet hasten the onset, whilst warmth and rest postpone the time of appearance of the typical symptoms.

A connexion between food consumption and the time of onset of the disease was thus indicated. Some experiments by Braddon and Cooper, in 1914, to ascertain if such a relationship existed were not completed, but showed a quantitative relationship. No other direct work on these lines seems to have been done. The Report on Vitamins of the Medical Research Council, though it mentions the work of Braddon and Cooper, simply gives the impression that a certain daily quantity of vitamin B is required, irrespective of the quantity of the food.

On this basis of a definite daily quantity my first experiments were made. They were carried out in conjunction with Dr. Rosedale, who has been a partner in all subsequent work. The attempt was made to rear chicks from day-old to maturity on a diet of oatmeal and the three vitamins. A definite daily quantity of yeast extract to supply vitamin B was added to the food. As the chicks grew older and increased in size they required more food. This was supplied by extra oatmeal without adding more yeast extract. The birds became ill, and were found to be suffering from polyneuritis. They were cured by dosing them with yeast extract. By adding vitamin B in the original proportion to the whole of the oatmeal consumed the birds were then raised to maturity without trouble.

A further observation was made that if the cod-liver oil of the diet was increased it adversely affected the birds. Their health was restored by an increase of yeast extract.

Later, using white rice in place of oatmeal and the same proportion of yeast extract, it was again found that the birds became affected with polyneuritis, but that they could be reared if more yeast extract was given. On the oatmeal diet 1.5 per cent. was wanted, on rice 8.6 per cent., from which one could calculate that oatmeal itself contained an equivalent of 7.9 per cent. of yeast extract.

A quantitative relationship between vitamin B and the carbohydrate in the food was thus clearly indicated, and has seemed to us to be of such fundamental importance in nutrition that our work during the past two years has been devoted to testing out this question of proportion with the three classes of foodstuffs: protein, fat and carbohydrate.

The first and longest series of experiments has been made with protein.

It had been found that on a diet consisting of—

White rice	Yeast extract	Cod-liver oil	Fishmeal
90	9	1	5

chicks could be raised without trouble to maturity.

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Excess of protein was added, so that the diet became—

White rice	Yeast extract	Cod-liver oil	Fishmeal
90	9	1	30

Two groups of chicks were started, one on the control diet with 5, and the other with 30 parts of protein.

Out of eight birds in each group only two were raised on the 30 parts of fishmeal, and these were ill with leg weakness. With 5 parts of fishmeal five were reared, but they showed slight signs of leg weakness. The cause of the losses could not be accounted for at the time, but it was afterwards found to be due to the yeast extract, which was not so good as that used previously.

In order to ascertain whether the protein of the diet wanted vitamin B to balance it further groups were started in turn with more yeast extract in the diet. The diets of these groups were thus:—

White rice	Yeast extract	Cod-liver oil	Fishmeal
90	12	1	30
90	14	1	30
90	16	1	30

With 12 parts of yeast extract there were three losses out of ten; with 14 parts one loss out of twelve, and with 16 there were six losses.

A group was then started on the original diet with 10 parts of yeast extract; there were six losses out of eleven, which pointed to a lower content of vitamin B in the yeast extract. The birds reared on the high protein diet were not altogether normal, as they showed bow legs or knock-knees. There was a possibility that this deformity was due to the high salt content of the diet arising from the fishmeal and the yeast extract, so that a series was started on diets with dried yeast instead of yeast extract. On the higher amounts of yeast all the birds were reared, but some losses occurred with the lowest amount of yeast. In every group there were some cases of leg abnormality. As the salt could now be excluded, the cause was believed to be the high protein in the diet. To investigate this point another series was started with a constant yeast diet, but with increasing protein. The series was:—

White rice	Dried yeast	Cod-liver oil	Fishmeal
90	20	1	5
90	20	1	10
90	20	1	15
90	20	1	20
90	20	1	25
90	20	1	30
110	20	1	5

with a control with low fishmeal and extra rice to correspond with 30 parts of fishmeal. With one exception, in the case of 10 parts of fishmeal, all the birds were reared and were quite normal up to a quantity of 15 parts of fishmeal. With 20, 25 and 30 parts of fishmeal, the birds were pale, shaky and had crooked legs. The crooked legs were apparently due to the high protein, but the other symptoms pointed to insufficiency of yeast in the diet. In the control group there were four losses out of twelve birds. It was possible that some of the leg trouble was due to insufficiency of cod-liver oil, and a further set was made to test this with diets containing 2 per cent. of cod-liver oil. The results were similar. The bow legs or knock-knees were thus mainly due to the high protein of itself. It seems impossible to test the problem quite satisfactorily. Comparing the appearance of the birds and the cause of the losses it seemed almost certain that the protein of the diet wants balancing by vitamin B. It is not possible

to indicate the poor appearance of the birds on the low yeast diets by photographs. Excluding the deformity, the birds were pale and not in the condition seen with birds on a good diet. There were some distinct cases of leg weakness as seen in polyneuritis.

HIGH FAT DIETS.

The results on high fat diets were more satisfactory in regard to the need of balancing the fat of the food with vitamin B. In these experiments, cotton-seed oil was used to produce the high fat content. The series of diets was:—

White rice.		Dried yeast.		Cod-liver oil.		Fishmeal.		Cotton-seed oil.
58	...	12	...	2	...	8	...	20
54	...	16	...	2	...	8	...	20
50	...	20	...	2	...	8	...	20
60	...	10	...	2	...	8	...	20

The first experiment showed no losses in the group, but the birds were quite abnormal throughout the time of the experiment. They were always dirty and oily from the first week, and later showed very poor feathering, with some slight signs of leg weakness. At the end, at twenty weeks, several birds were almost naked. With increase in the dried yeast, the dirty appearance was never seen, and the feathering was quite normal. The next experiment was tried to see if more yeast was of greater benefit, but the result showed no advantage. The last experiment has just been begun on still less yeast; in the first week the oily appearance is noticeable. Though no deaths have occurred, the need for extra yeast to balance the fat was quite evident. In all experiments the high oil of the diet depresses the growth below the normal; it was more marked with the low yeast.

HIGH CARBOHYDRATE.

Finally, experiments were made to test whether the carbohydrate wanted balancing by yeast as proof of our former work with oatmeal and rice.

The experiments have been carried out with a decreasing amount of dried yeast in the diet:—

White rice.		Dried yeast.		Cod-liver oil.		Fishmeal.
74	...	16	...	2	...	8
78	...	12	...	2	...	8
80	...	10	...	2	...	8
82	...	8	...	2	...	8
84	...	6	...	2	...	8

In the first two groups, the birds reached maturity in perfect condition. With 10 parts of yeast the birds have looked pale and at maturity were not in such perfect condition as on the higher amounts. With 8 parts of yeast, there was only one loss, but the birds were very pale, and at maturity two of the cock-birds were slightly deformed. When killed, the cocks were found to be very fat in the abdominal area with the gizzard covered with fat. With 6 parts the birds were still paler; the experiment is still in progress and the birds look distinctly ill. As far as condition is concerned, the diets with 16 and 12 parts of yeast are by far the best. It might be said that 12 parts of yeast are really the minimum for perfect health, though birds can be reared on 10 and 8 parts.

PIGEONS.

Some other experiments with pigeons show the need of balancing the carbohydrate of the food more clearly. Pairs of pigeons have been kept on a diet containing 5 per cent. fishmeal, 2, 4, 5, 6, or 8 per cent. of yeast extract and the remainder white flour. Except those on 8 parts of yeast extract, all have died within twenty weeks, showing typical symptoms of polyneuritis. With 8 parts of yeast extract, the cock-bird died in the twenty-ninth week, showing no symptoms beyond an enlarged heart. The hen-bird is living at the thirty-fifth week.

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RATS.

It was of importance to ascertain whether rats had the same requirements as pigeons. Rats have been kept on 1 part cod-liver oil, 5 parts fishmeal, 0, 1, 2, 4 parts yeast extract and the remainder white flour.

With 0 parts of yeast extract, the rats lived for nineteen weeks. With 1 part they are alive after nearly forty weeks; they have had two lots of young, which the mother has promptly eaten. With 2 parts, the rats were kept for over six months; they had young about every six weeks and the young have been eaten. With 4 parts the rats have reproduced and have brought up their young. The balance of carbohydrate by vitamin B is thus clearly indicated.

It is not possible to say what are the requirements for man. Pigeons want more than rats and other birds want more than pigeons. Some experiments with cats indicated that larger amounts are wanted than are needed by rats. For safety, therefore, it would be best to regard the amounts for pigeons as those necessary for man.

Similar views about the balance of food by vitamin B have been expressed by the French workers, Randoi and Simonet, who show the relationship by the

$$\text{Ratio} \frac{\text{vitamin B}}{\text{carbohydrate}} = \text{constant.}$$

Our work shows that the relationship should be:—

$$\frac{\text{Vitamin B}}{\text{Total food (calories)}} = \text{constant.}$$

Perhaps the chief interest to you in these experiments is the cause of death of the birds in the various groups. Only in a few cases were the typical symptoms of polyneuritis observed. Post-mortem examination of the birds which died without these symptoms has always shown the large intestine filled either with hard compact masses of food residues, or with pasty masses, often extending into the small intestine. The appendices were also usually filled with masses of decomposing food. The livers were sometimes pale, and the hearts enlarged. Occasionally the body cavity and peritoneum have been found filled with liquid, or coagulated serum. The symptoms have not been severe enough to produce real inflammation of the intestine or appendices. It would seem that death was due to poisoning from the putrid food residues in the gut. The condition of the birds was more one of chronic ill-health than of any acute illness.

These symptoms correspond with those described by McCarrison as occurring in the early stages of polyneuritis. The difference is that these symptoms are chronic, associated with diets containing a shortage of vitamin B, whilst in polyneuritis they represent a short intermediate stage rapidly followed by paralysis and other typical symptoms of beri-beri.

The effect of shortage of vitamin B differs from that due to its absence in leading only as far as the intermediate stages.

We suggest that this intermediate condition is the point at which an unknown chemical agent enters which is supposed to be a factor in the onset of diseases such as cancer. The unknown chemical agent may be a toxin absorbed from the putrid contents of the gut.

It will have been noticed that large amounts of yeast, of the order of 10 to 12 per cent., have been required in the food to ensure perfect health. For practical purposes in human nutrition, it is necessary to inquire whether the ordinary food-stuffs contain enough vitamin B to balance the food and to ensure perfect health.

There are a few comparative data of ordinary foods drawn up by Cooper and by Chick and Hume. These data do not include wheat and other cereals. Our work has also consisted in testing some of the common foods for their vitamin B value.

For this purpose we have used pairs of pigeons, and the test of the food has been long maintenance on it for one, to two years with reproduction. The cereal has first been given to the birds and then after reproduction it has been diluted with 10, 20, 30 per cent. of white rice. A stage has thus been reached at which the eggs of the birds have not hatched, or no eggs have been laid. The results of these experiments may be given in a table:—

	75 per cent.	balances	25 per cent.	of white rice
Wholemeal flour, maize
Rye	55	"	45	"
Barley	65	"	35	"
Millet, dari	60	"	40	"
Bran, middlings	30	"	70	"
Wheat germ, yeast extract	10	"	90	"
Potato	90	"	10	"
Peas, dried	40	"	60	"

The data show that a diet must contain 75 per cent. of whole wheat to ensure health and reproduction; with oatmeal the amount must be 95 per cent., &c. From these data it may be concluded that the ordinary daily diet in this country does not contain enough vitamin B, and the ordinary minor troubles of the population, such as constipation and gastro-intestinal troubles which correspond with shortage of vitamin B, thus arise.

New Facts Concerning the Fat-soluble Vitamins.

By J. C. DRUMMOND, D.Sc., F.I.C.

CONSIDERABLE progress in the study of the fat-soluble vitamins has been made since McCollum and Osborne and Mendel in 1913 first observed the marked influence on growth which certain animal fats exhibit in contrast to the inactivity of the majority of vegetable oils.

For a number of years it was considered that this physiological action of animal fats was due to the presence of a substance to which the name "fat-soluble A" was given. It was demonstrated quite clearly by extensive experiments in America and Great Britain that this substance, whatever its nature, is essential for the growth and well-being of young animals, but it was not until E. Mellanby carried out his well-known researches on the causation of rickets that the influence of certain food-stuffs in facilitating the disposition of lime in developing bone was traced to a dietary factor of the same type.

THE ÆTIOLOGY OF RICKETS.

It will be remembered that at the time Mellanby published his researches there were two conflicting schools of thought regarding the ætiology of rickets. On the one hand a considerable number of authorities regarded the disease as being primarily due to defective hygienic surroundings, in particular lack of sunshine and exercise, whilst on the other certain observers were inclined to regard it as due to defective diet. The experiments of Mellanby made it clear that rickets can be produced at will in experimental animals by depriving them of a dietary constituent similar, as regards its distribution in natural foodstuffs and its general properties, to the vitamin that had been discovered by the American investigators in 1913.

Mellanby was careful not to assume the identity of the two factors, and for a period there was some confusion in the minds of scientists as to whether the growth-promoting and antirachitic properties of a foodstuff such as cod-liver oil were due to one or more than one factor.

We owe it to the researches of McCollum at Johns Hopkins University, Baltimore, that a clear differentiation between the substances responsible for these two effects

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was made. McCollum demonstrated that the rate of destruction of the growth-promoting and antirachitic potency of cod-liver oil were destroyed at very different rates by subjecting the oil to oxidation. Furthermore, he ascertained that certain natural foodstuffs may show powerful activity in preventing rickets without any marked effect on growth or vice versa. It appeared very probable, therefore, that at least two substances of the fat-soluble vitamin type occur in cod-liver oil, and for purposes of classification these are to-day termed vitamin A and vitamin D, the former term being applied to the substance more particularly affecting growth, and the latter referring to the factor playing a part in the deposition of lime in bones.

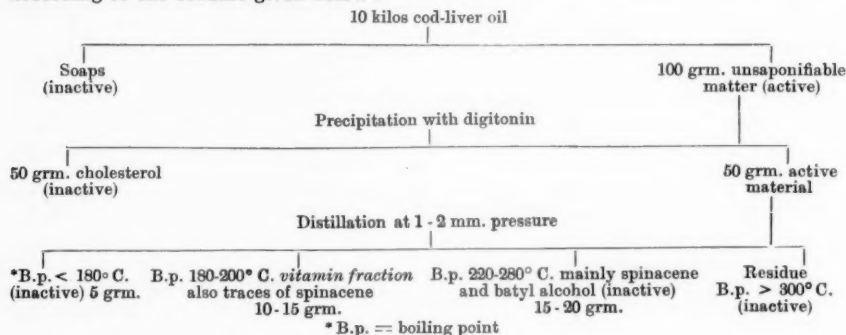
A NEW FAT-SOLUBLE VITAMIN.

Before passing on to consider in detail recent investigations regarding these two interesting subjects, I should like to draw attention to the important researches by Professor H. E. Evans, of California, which have proved the existence of a third vitamin of the fat-soluble class playing an extremely important part in reproduction. As yet information concerning the chemical nature of this substance is meagre, but in my laboratory we have satisfied ourselves that the factor discovered by Evans is distinct from either vitamin A or D, and we have confirmed his main conclusions regarding its action. This newly discovered factor is now termed vitamin E. It is, I think, a most interesting fact that the attention of both biochemists and physiologists is at the present time being diverted from the true fats themselves, and is being directed to the examination of the small traces of substances which usually accompany the glycerides as they occur naturally.

It will be remembered that the majority of natural oils and fats, such as cod-liver oil, consist of about 99 per cent. true fats—i.e., glycerides—and some 1 per cent. substances which resist the action of potash when fats are broken down into glycerol and soap in the ordinary saponification process. This 1 per cent. is termed the unsaponifiable matter. In the past this fraction has attracted very little notice, and interest has centred entirely round the digestibility and nutritive value of the large proportion of true fats present in the oils. The discovery that the unsaponifiable fraction (if prepared with care so as to prevent secondary changes, in particular oxidation, occurring) contains the whole of the vitamins present in the original oil has, as I say, diverted attention to the examination of this fraction.

THE NATURE OF VITAMIN A.

I will first bring to your notice some few details of our own attempts to isolate and to determine the nature of the vitamin A, which appears to be largely responsible for the beneficial influence which cod-liver oil exercises on growth. The unsaponifiable matter prepared from cod-liver oil has been submitted to chemical fractionation according to the scheme given below:—



From this table it will be observed that we have succeeded in separating the active substance from a number of other constituents of unsaponifiable matter, but I regret to say we have not yet achieved the separation of the vitamin A in what can be considered to be the pure condition.

Some of you will recall a statement in the lay press a few weeks ago that the Japanese investigator, Takahashi, had succeeded in isolating vitamin A as a pure compound. We have critically examined his work and have satisfied ourselves that his preparations are not more pure than those which we have obtained. It may be of interest to discuss the rather extraordinary potency of the preparations which have been obtained by this fractionation.

The experimental animals employed in these investigations are usually rats. A rat of 100 gm. body-weight will consume during the day approximately 15 gm. dry weight of food. If this food be deficient in vitamin A the animal will completely fail to grow, and in due course will decline in weight and die. In order to keep the rat alive, to maintain health, and to permit a normal rate of growth, it is only necessary, as we have found, to supplement his deficient diet with an amount of active fraction weighing 200th mgm. You will, I think, agree with me that this dosage is of so small an order as to recall the effective doses of internal secretions and of certain drugs.

I fear I cannot give any clear idea, as yet, of the chemical nature of vitamin A, but the very highly active fractions we have obtained largely consist of unsaturated higher alcohols, containing in their molecules only the elements carbon, hydrogen and oxygen. It is possible that the vitamin is actually one of these alcohols, but until we have prepared it in undeniably pure condition it would be unwise to draw such a conclusion. It will be agreed, at any rate, that we must abandon all ideas of the vitamin being a labile, ill-defined compound, such as we at one time imagined it to be when it is so readily demonstrated that it can survive such drastic chemical treatment as saponification with boiling alkalies and distillation at temperatures over 200° C.

I will not say more about vitamin A beyond mentioning that Dr. O. Rosenheim and I have recently described a simple colour reaction which we believe is caused by it and which is proving of great use in detecting the presence of the active substance. I must now pass on to give a brief review of

RECENT KNOWLEDGE CONCERNING VITAMIN D.

As pointed out above, McCollum's work clearly differentiated vitamin A from vitamin D, but this advance did not at once help to reconcile the two conflicting schools of thought regarding the causation of rickets. The reconciliation seems to-day to have been accomplished, and the story of its achievement is one of the most fascinating presented by recent scientific progress.

In 1919 Huldshinsky observed that children suffering from rickets were rapidly cured on exposure to sunlight, or to the light of lamps which emit rays in the ultra-violet part of the spectrum. This striking observation soon received general confirmation, and some glimpse was then obtained of the line upon which one might correlate the views of the two opposing groups of scientists. But, welcome as some prospect of clearing up this difficult matter was, there still remained the task of determining why rickets could be cured equally well by exposing the patient to ultra-violet light or by administering a substance such as cod-liver oil.

The first clue that led to a solution of this problem was provided by the careful work of the American investigator Steenbock, who discovered the remarkable fact that a food mixture which, by reason of its deficiency will give rise to rickets in animals, becomes endowed with antirachitic potency after it has been exposed to ultra-violet light. Two possibilities suggested themselves to account for this. On the one hand, it was possible that the treated fats absorbed ultra-violet rays, and that

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the energy so absorbed was later emitted in the form of secondary radiations, which effected a curative action similar in character to that produced by direct exposure to the primary radiations. On the other hand—and it seemed a more attractive hypothesis—it was possible that the absorption of the short wave-length radiation actually produced in the foodstuffs a substance of the type of antirachitic vitamin D. It was comparatively an easy matter to examine one by one the constituents of the food mixture, and this examination soon revealed that the precursor of the physiologically active substance is present in the oil or fats. The examination of such activated fats revealed that the conference of antirachitic potency could be traced to the action of ultra-violet light on a constituent or constituents of the unsaponifiable fraction. One of the most commonly occurring substances in these unsaponifiable oils and fats is the familiar substance cholesterol—a substance of almost universal distribution in living cells.

Dr. Rosenheim, Mr. T. A. Webster and myself were able to show, simultaneously with Steenbock and Hess in the United States, that cholesterol, or the very closely related compound, phytosterol, is the parent substance of the antirachitic vitamin. It is possible to take the purest specimens of cholesterol—and it is a substance which can be prepared in a state of considerable purity—to expose it to ultra-violet light for an hour or two under suitable conditions, and to obtain thereby a product showing an extremely powerful antirachitic action. This activated cholesterol, if we may so term it, shows little or no effect on growth, nor does it show other properties of vitamin A, so that it may now be definitely accepted that these two substances A and D are distinct.

As yet the chemical investigation of the substance produced from cholesterol by the action of ultra-violet light has not revealed the chemical nature of the active substance. It should, however, prove possible to obtain a fairly large amount of this material, to fractionate by some such process as I have already described, and then to obtain the antirachitic substance in a pure state and ascertain its nature and properties.

I have presented these questions very much from the biochemical aspect. I have done this because I am in my own researches primarily concerned with the biochemical problem of determining the chemical nature of these remarkable substances and ascertaining their physiological action, and I shall be satisfied if I have made clear the following points.

In the first place, there can be no question, I think, that there has been satisfactory differentiation between these two fat-soluble vitamins A and D, and that both of them appear to be physiologically efficient in amounts so minute compared with the quantities of ordinary foodstuffs that are required by the body, that in looking for parallels one can only call to mind the action of agents such as the secretion of the thyroid gland or of certain drugs. In the second place, I hope that I have dissipated from the minds of any who still retain it the old and erroneous idea that the vitamins are hypothetical substances, or that, if they exist, they are substances of ill-defined character comparable with the enzymes or the toxins.

Discussion.—Dr. M. J. ROWLANDS said he was very pleased to have the opportunity of opening the discussion as he had watched the experiments of Professor Plimmer on animals with interest and the result of the work at St. Thomas's Hospital. He had also had the pleasure of travelling round England with Professor Drummond when his original work began. He (Dr. Rowlands) had thoroughly investigated the question of vitamins, upon which, commercially, he had spent large sums, and they had yielded a successful return as the result of the knowledge he had gained on the work of both Professor Plimmer and Dr. Drummond.

He wished that Professor Plimmer had discussed the question of intestinal toxæmia in relation to vitamin B a little more fully. It was a well-known fact that beri-beri was not of common occurrence in human beings for the reasons Professor Plimmer had stated, but the

question of intestinal toxæmia and deficiency of vitamins was so marked to-day that cognizance of vitamin B in relation to digestion and intestinal toxæmia was of the utmost importance. He was not in any way questioning the accuracy of Professor Plimmer's figures or experiments as he had shown definitely that the balancing of our diet was most important, and he (Dr. Rowlands) had come to the conclusion that the majority of the troubles of patients were chiefly intestinal in origin due to a vitamin deficiency.

Dr. W. H. ANDREWS said he did not know to what extent animals living under natural conditions might sometimes be forced to live on a diet which was deficient in vitamins, or if such conditions ever occurred at all, but he thought it unlikely that animals which actually grazed on natural pasture ever suffered seriously in this respect. We had to recognize, however, that most of our domestic animals did not receive a natural diet, and the tendency to keep them on diets which were not altogether natural was increasing.

Of the diseases which were recognized to be due to serious vitamin deficiency, rickets was the only one which (as far as he was aware) was encountered in the domesticated animals. Polyneuritis might occur, of course, in domesticated birds, but in the ordinary domestic mammals we did not meet with anything like polyneuritis, beri-beri or scurvy. For this reason he was particularly interested in Professor Plimmer's account of the effects brought about by a more moderate deficiency of vitamin B. Such ill-defined disturbances of digestion were, as was known, extremely common in man, and we had plenty of that sort of thing in the domestic animals also.

We did not know much about the vitamin requirements of the domestic herbivora, but it seemed to be difficult to induce in them any well-defined avitaminosis. He had not worked on this subject himself, but he had had the privilege of watching two different series of experiments of this nature.

In the first case, the experiments had been carried out in South Africa by Mr. A. Stead, who was endeavouring to show that the disease "lamziekte" in cattle was the bovine equivalent of beri-beri. "Lamziekte" was not induced, but after a time the cattle developed laminitis.

The second series of experiments had been performed by Sir A. Theiler and his co-workers, and both horses and cattle were fed over prolonged periods of time on diets which were very seriously deficient (as judged by the usual standards) in vitamin B.

Here, again, no well-defined avitaminosis had been induced, but some of these animals also developed laminitis. One could hardly regard laminitis as a form of avitaminosis; it was a condition with which they were all very familiar, and it often arose in animals which were undoubtedly getting ample supplies of all the well-recognized vitamins. For example, he had seen a considerable number of severe cases during the war in horses which were suddenly placed on full rations of wheat; these horses were receiving also generous rations of fresh green food, and there could not have been any vitamin deficiency. We had to assume that the animals which developed laminitis, when given diets which were deficient in vitamin B, were affected by some other factor connected with the food. We recognized that horses, and less commonly cattle also, were more likely to suffer from laminitis when receiving food which was in some way (quite unconnected with its vitamin content) unsuitable, or to which the animals were unaccustomed. This point was well illustrated in the war experience to which he had already referred; all of the horses of a particular force had to be placed on a wheat ration, as oats and maize were not available; the horses which were given large amounts of wheat, without previous preparation, suffered from serious digestive disturbance, and in many cases developed laminitis, but those which received at first only small amounts soon became accustomed to it, and when the amount was gradually increased they could be taught to tolerate, and indeed to thrive on, the full ration.

It certainly seemed that adult cattle and horses required only an extremely small proportion of vitamin B, and he supposed that at present there was no actual proof that they required any at all; the requirements of the young and actively growing animals were, of course, in a different category, but he did not know of any attempts to determine them.

Dr. KINGSTON BARTON asked what was meant by the recommendation of ultra-violet rays and artificial light as a means of curing rickets. Formerly, when he had to treat numerous cases of rickets amongst both the poor and the well-to-do of London, he became convinced that the main factor in the causation of rickets in children consisted chiefly in the wrong diet of suckling children. He fully believed that there was a vitamin factor in this nutritional disorder, but he could not accept the statement that all rickets could be cured by ultra-violet

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rays and by simply exposing foods and oils to irradiation. The rickets of rats, the animals usually selected for all the experiments, was in his opinion not comparable. For in rats extreme rickets could be produced in a very few weeks when the improper diet was given. It was generally reported that the bony changes seen in rickets were cured whilst the animals were subjected to the light treatment. But all the same, if the wrong diet went on the animals died, so there was no great advantage in "dying cured." In the human subject rickets took quite a number of months to develop even when very inappropriate diet was given, so it was inconceivable that light alone could possibly cure rickets unless there was also the most careful attention given to the dietary, which always depended on the age of the child thus suffering. Even in this cloudy country he thought there was enough sunshine to cure rickets if only the diet was planned rightly.

Rather than the promulgation of these ideas extremely expensive of artificial lights, he thought that the public should be instructed as to what vegetable or meat food contained the proper amount of vitamins, whether A, B or C.

With regard to intestinal troubles, we had hitherto been told by bacterial experts that they were entirely due to great excess of streptococci, or of the *Bacilli coli*, and that the only remedies of value were vaccines. But in a recent paper by Dr. Lawrence Garrod, in the *St. Bartholomew's Hospital Reports*, 1925, it was stated that a reduction in the carbohydrate intake would very speedily get rid of all the streptococci, and that a diminution in protein diets would lead to an elimination of all the *Bacillus coli* groups from the intestine. But Professor Plimmer had presented an altogether new idea, namely, that the vitamin B was the potent factor in prevention of all these intestinal disorders. This at all events was a more simple explanation, for yeast was a vitamin that could be obtained cheaply. It was interesting to observe for how many years country housewives used to treat members of their households suffering from boils and other suppurations by giving them yeast daily with their food.

Professor DRUMMOND (in reply) said that Miss Chick showed that children can be cured either by exposure to ultra-violet light or by giving them suitable food. One speaker had asked whether he was to understand that vitamin A was actually produced after radiation. Such was not the case. Only the antirachitic vitamin D was produced by exposure of an inactive oil, such as cotton-seed oil, to the ultra-violet rays.

He said he was himself responsible for a certain amount of the confusion because we found that cholesterol after irradiation had a stimulating effect on growth.

Eventually the inter-relationship of the two vitamins A and D and their effects on growth were being cleared up and we began to obtain some idea of how they acted. He himself was quite satisfied that there was no question of a production of vitamin A from cholesterol by the action of ultra-violet light.

Section of Comparative Medicine.

President—Mr. FREDERICK T. G. HOBDAY, C.M.G., F.R.C.V.S.

The Relation of Wild Animals to Certain Diseases of Man.

By P. H. MANSON-BAHR, C.M.G., M.D.

IN the highly civilized state to which the majority of mankind has attained at the present day, it is only in the tropics, where he still exists in a more or less primitive state, that an intimate contact with the indigenous fauna is possible; and it is therefore mainly in tropical countries that we find him a prey to disease germs which normally infest wild animals. Probably, at one time, some of these parasites were more widely spread than at present; but the exact manner in which they originated still remains a matter for speculation. It is probable, too, that primarily their virulence was much greater, but that, in process of time, each species of animal became tolerant of each particular parasite, so that eventually a state was attained in which host and parasite existed on terms of harmony; this is a condition such as we understand by the "reservoir" state; but it is one in which the parasite retains its virulence for non-immune individuals.

There is hardly a subject which so strongly supports the Darwinian hypothesis of the origin of man as this, and it is one which Darwin himself, had he been familiar with the details, would doubtlessly have exploited to the full. That man is in fact but part and parcel of the great scheme of Nature and heir to the parasitic infections of animals around him, and a victim to parasites which fulfil their purpose by destroying or checking the numbers of immigrant species, appears to us now to be a self-evident fact.

For the passage of these disease germs from one host to another prolonged and intimate contact is necessary, but when once this chain of contact is broken, the parasite is no longer able to attain the different stages necessary for its evolution and must perish. But in the process of civilization certain animals such as the ox, the pig and dog, have during domestication inherited diseases from their wild ancestors and have continued to transmit them to man, who in turn has become, in some cases, the necessary intermediary host. The theories as to how these disease germs arose in the first instance, and how they became adapted to man, we will discuss at a later stage.

TRYPANOSOMIASIS.

The trypanosomes are blood parasites of many diverse orders of the animal kingdom; they attain their greatest development in the continent of Africa, where they exist as apparently harmless commensals in the blood of the larger ruminants, especially the antelope of that country. These organisms have become adapted to very varied conditions, and species peculiar to birds, reptiles, fishes and amphibia are known.

In Africa, man has become infected with only two species which infest mammalia, viz., *Trypanosoma gambiense* and *Trypanosoma rhodesiense*. In South America a perfectly distinct species, *Trypanosoma cruzi*, has been found parasitic in man in certain limited areas in Brazil and Venezuela.

Trypanosoma gambiense is responsible for the best known form of sleeping sickness in man; it is indigenous and peculiar to Central Africa, where it has spread as an epidemic over a vast area during the last half century. The range of this disease is coterminous with that of the tsetse-fly, *Glossina palpalis*, which acts as its definite host. Under laboratory conditions, this trypanosome can be conveyed to most domestic animals, to monkeys and the larger antelopes, but there is a good deal of evidence that at the present day it is essentially a human infection and is spread by the agency of man to man. There is, however, one antelope which, from its habits and its range, is admirably adapted to act as a reservoir of *Trypanosoma gambiense*. This is Speke's sitatunga (*Limnotragus spekei* [2], or *Tragelaphus selousi*), of which naturally infected individuals have been found by Duke [3] on the Sesse Islands in Lake Victoria. This very handsome antelope stands 36 in. at the withers. The buck possesses fine spirally twisted horns. In ground colour it is of a uniform greyish-brown, but the head is adorned with white ocular and cheek spots and a white chin. The type species comes from the Sesse Islands, but minor variations have been traced throughout its range which extends through the lakes and swamps of Eastern and Central Africa. This species, which was discovered originally by Speke in 1861, is a very wary antelope, and as it lives in dense and impenetrable papyrus, it is rarely seen or shot by Europeans. It occurs in the greatest numbers on the islands already mentioned, which from the year 1900 onwards were ravaged by sleeping sickness to such an extent that in 1909 the inhabitants were moved to the mainland. Five years [4] subsequently the tsetses of the island were still found to be infected with *Trypanosoma gambiense*, a fact which was attributed by Duke to the presence of infected antelopes of this species. The hoofs of this antelope are long and widely splayed, an admirable adaptation to its habitat, but since the removal of the population from the islands already referred to it has come to live on dry land and its hoofs have become much shorter and modified accordingly.

The sleeping sickness of man produced by *Trypanosoma rhodesiense* does not differ essentially from that produced by the former species. On the whole the illness runs a much more rapid course, and is accentuated by severe febrile paroxysms. Fatal symptoms usually supervene within a year of infection. The organism is much more resistant to drug treatment, especially the arsenical compounds, which have been found efficacious in *Trypanosoma gambiense* infections. This disease has a curious distribution in Central Africa, for it corresponds very closely to that of *Glossina morsitans*—the tsetse of the big game; but it never appears to spread in man in epidemic form. This sleeping sickness occurs in North-Eastern Rhodesia, especially in the Luangwa Valley, in the south-eastern portion of Tanganyika territory, in Nyasaland in the region south and west of the lake. Whilst present in the blood of man, *Trypanosoma rhodesiense* is indistinguishable from *Trypanosoma gambiense*, but it was differentiated by Stephens and Fantham in 1910 by the fact that when inoculated into laboratory animals, especially the rat, a change takes place in the trypomastix, which assumes a position close to the kinetoplast or sometimes posterior to it. Subinoculations into laboratory animals are invariably successful and run a rapid and fatal course, in contradistinction to what happens in the case of *Trypanosoma gambiense*.

The part played in the dissemination by the wild game of this parasite to man has been the subject of a great diversity of opinion.

The trypanosome of the big game in this area, *Trypanosoma brucei*, belongs to the polymorphic group of trypanosomes and is indistinguishable, morphologically, from *Trypanosoma rhodesiense*. Yorke, Kinghorn, and Bruce believe that under certain conditions *Trypanosoma brucei* can be inoculated into man and produce a *rhodesiense* infection, but others, notably Kleine, Taute and Huber, by experiments upon themselves, either by injecting themselves with *Trypanosoma brucei* infected blood, or

through being bitten by infected *Glossina morsitans*, without contracting the disease, consider them specifically distinct. It is, however, clear that a large proportion of the game must be infected with *Trypanosoma rhodesiense*. Waterbuck (Week [5] 1914) have been infected with human *Trypanosoma rhodesiense* and have shown no signs of disease, though this animal's blood produced in turn a fatal infection in monkeys and dogs.

Three species of antelopes are usually regarded as reservoir hosts of *Trypanosoma rhodesiense*. The handsome common waterbuck (*Cobus ellipsiprymus*, Ogilby) [6] has a wide distribution in Central Africa; its range extends from the Limpopo River northwards to Tanganyika Territory and Kenya, as far north as Somaliland; on the west it is replaced by allied species. The waterbuck is readily distinguished from others by the white ribbon which passes over the rump and is carried down the thighs on both sides. Although it has the appearance of a clumsy animal, it becomes elegant and sprightly when excited. It can travel at a fast gallop and is difficult for man to follow, though falling an easy prey to lions and leopards.

The waterbuck is always found in greatest numbers on large swampy plains overgrown with coarse grass, tall reeds and papyrus, where in the wet season it is impossible to get at it. It revels in almost inaccessible swamps where only elephants, buffaloes and reedbucks care to stay. For this purpose Nature has provided the waterbuck with a tougher hide and coarser hair than any other of its kind, so as to protect it against the sharp fronds of papyrus and other water plants. From the nature of its habitat it will be understood that the extermination of the species would form an almost impossible task.

The reedbuck (*Cervicapra arundinum*, Bodd) [7] is a comparatively large antelope measuring some 36 in. at the withers, and in general colour greyish-fawn. It has a thick and bushy tail reaching half-way to the hocks, and handsome evenly divergent horns which curve backwards and upwards. The female resembles the male, but is hornless. There are at least five species of varieties of the reedbuck. Rare in the Transvaal and Bechuanaland, it is still plentiful around Lake Nyasa, and extends as far north as Mozambique and on the west to Angola. This antelope is easily approached, its gallop is slow and irregular, and it is said to be one of the easiest of the South African antelopes to shoot. When alarmed the herd give vent to shrill screams and bound off, kicking up their hind legs and tossing their tails like rabbits. It has not been found possible to keep this species in captivity.

There are many species of *Duikerbuck*; the majority are at home in the dense bush of Western Africa. The common duiker, *Cephalopus grimmii* (Linn.) [8] was originally described by Grimm in 1686, and has a wide distribution throughout the *rhodesiense* sleeping sickness area, being found throughout South Africa, along the east coast as far north as Somaliland. It stands 23 in. height, the general colour of the body being pale greenish-brown. Horns are normally present only in the male, in whom they attain a length of 5 in. This antelope is called the "duiker," or diver, not from its habit of going into water, but from its manner of ducking and diving quickly into bushes when alarmed. In the Cape it is frequently kept in a semi-domesticated state around farmhouses, but does not thrive in captivity in this country.

SOUTH AMERICAN TRYPANOSOMIASIS.

Caused by *Trypanosoma* (*Schizo-trypanum*) *cruzi*, this disease runs a very different course, and has an entirely peculiar natural history. This parasite causes a chronic or acute disease in children, especially in certain districts of Brazil and Venezuela. The symptoms partake for the most part of a myxoedematous [9] character, with febrile disturbances and enlargement of the thyroid gland. The chronic stage may also be seen in adults, when it is characterized by organic syndromes, due to the involvement of the heart muscle, suprarenal glands, or nervous system. The parasite

occurs in the blood-stream in forms which are said to represent young individuals which have just escaped into the circulation, and in broader ones representing an older generation. Multiplication of the parasite by leishmania-like forms takes place in most of the tissues of the body, especially in the skeletal and cardiac muscles.

The infection is disseminated by curious reduviid bugs, the most important of which is *Triatoma megista*; this bug constitutes the definitive host of the parasite. A large proportion of these insects are found to be naturally infected; they live entirely on wild animals, such as armadilloes, whose burrows they frequent, but certain species have become domesticated. Both the larvæ and the nymphs of this insect can become infected with *Trypanosoma cruzi*. Considering the wide range of these bugs, and the facts (1) that certain species are found naturally infected with this trypanosome in Argentina, (2) that an allied form, *Triatoma protracta*, is found in a similar condition in the United States, (3) the ease with which the parasite can develop in other insects (*Cimex* and *Ornithodorus*),—it becomes difficult to comprehend the limited geographical distribution of this disease as it occurs in man. The trypanosome is probably under natural conditions conveyed to animals upon which the *Triatoma* feeds, and they therefore constitute the reservoir host. The most important are the armadilloes. The long-tailed armadillo (*Tatusia novemcincta*) [10] appears to be the natural host of *Trypanosoma cruzi*. This species inhabits Mexico and Central America, where it lives in burrows, but in Nicaragua is often kept tame in houses to protect them from invasion by ants. In Guatemala it abounds in primeval forests up to an altitude of 5,000 ft.; there it is much hunted for its flesh, which Dampier described as very sweet and tasting like that of a land turtle. When disturbed this armadillo rolls itself up like a hedgehog. Armadillo burrows are found underneath the houses, and in the immediate vicinity of these, cases of the human trypanosomiasis were originally discovered in Brazil.

The "peludo" (*Dasypus sexcinctus*) [11], a much smaller animal, 18 in. in length, common in Brazil, is an omnivorous creature, particularly fond of carrion. It is said to possess a faculty of burrowing up to a decaying carcase, in much the same manner as that of the ground-beetle. *Dasypus* has a very short tail, which is shielded by distinct rings near its base.

The other natural hosts of *Trypanosoma cruzi* are entirely different animals. The first of these is Azara's opossum (*Didelphys aurita*) [12], a marsupial which has a very extensive range in South America, from Uruguay to Costa Rica. This opossum creates the same havoc amongst poultry in these countries as does the fox in Europe. Sleepy and drowsy in the day time, the opossums live in the roofs of houses in intimate contact with man, rarely showing themselves in the open. In the towns there are few houses which are not infested with these hideous beasts. Often the stranger is roused from his slumbers by the sound which is caused by these animals running over the roof, upsetting in their course dishes and other household utensils. If he makes inquiry as to the cause of the alarm, he receives as an answer "Señor, es el zoro" (zoro is a fox in Spanish).

The fourth reservoir host of this interesting parasite is a rock cavy (*Cavia (Cerodon) rupestris*) [13], which is indigenous in Brazil in rocky situations. It is usually found near rivers, but always in the higher parts of their course, where it seeks its retreat in holes and amongst rocky boulders. Superior in size to most other caviæ, and standing higher on its legs, it is remarkable for the softness of its fur. It is 14 in. in length, and its flesh is said to be well flavoured and much sought after by the Indians. Brumpt and Gomes found infected triatomas in the burrows of this rodent in a deserted spot ten miles from any human habitation.

The history of this trypanosome is of comparatively recent date and is remarkable, not only for its peculiar life-history, but from the circumstances surrounding its discovery by Chagas in 1909. This observer first found trypanosome-like flagellates in the hind gut of triatomas, and Cruz, on causing these insects to bite

a monkey, subsequently found trypanosomes in its blood. It was this discovery which led Chagas to search for the trypanosome in the blood of man; in this he was successful in discovering it in the blood of individuals living in the very houses from which the infected triatomas were at first derived; there also he found the parasite in the blood of cats.

LEISHMANIASIS.

Parasites of the genus *Leishmania* are intracellular organisms, which, from a study of their structure inside the human body, as well as of their development into a flagellated stage in artificial media outside the body, are shown to be in close affinity with the trypanosomes. The *Leishmania donovani* is the parasite responsible for a generalized disease in man, known as kala-azar, which has a peculiarly restricted geographical distribution, being found widely spread in India (especially in Assam and the United Provinces), China (Central Provinces and the Valley of the Yangtse Kiang), Central Africa (Sudan, West Abyssinia and Tchad territory), along the shores of the Mediterranean basin, and in the Aegean Islands. In this latter area it is associated with a similar infection in dogs. The peculiarities of its distribution would seem to indicate that it is in some manner connected with the presence of some free-living reservoir host. The parasite can be communicated, though with difficulty, to dogs, cats, jackals, monkeys, rats and mice, but it is only lately that a really susceptible animal has been discovered. Smyly and Young have found that the hamster (*Cricetus griseus*) [14] is very readily infected; that in these animals an enormous proliferation of the parasite takes place. Apparently, in spite of the great numbers of the parasites, the health of these animals is not seriously affected. It therefore appears possible that this small rodent, or some similar animal, constitutes the reservoir host of the *Leishmania*, and that the actual transference of the parasite to the human body takes place through the agency of a small biting fly, such as the sand-fly, *Phlebotomus*.

The hamster, *Cricetus* (*Cricetulus griseus*, Milne-Edwards) [15] is a little species of the size of a field-mouse, and is common in the country districts round Peking and extends into Chinese Mongolia. This little creature makes extensive burrows, frequenting cornfields and destroying quantities of grain. Greyish-brown in colour, it is pale beneath, has large black eyes, and a median dorsal brown stripe.

WEIL'S DISEASE, AND INFECTIONS WITH LEPTOSPIRA.

A severe and fatal form of jaundice, associated with fever and a high mortality, has been known in Europe since it was first described by Weil in 1886. Its close resemblance on clinical grounds to yellow fever has long been recognized, so much so that, long before the true ætiological agent was discovered, it was known as Mediterranean yellow fever. The parasite, *Leptospira icterohæmorrhagiae*, was discovered in 1916 [16] by several Japanese investigators, and they were able to reproduce a typical jaundice in guinea-pigs. It has since been shown that this *Leptospira* is normally a parasite of a rat (*Rattus norvegicus* and *Rattus alexandrinus*) in Europe, and of the field vole (*Microtus montebelloi*) in Japan. In these animals apparently the organism lives in the urinary tubules of the kidney and is excreted in the urine. Thus it happens that large numbers of apparently healthy rats harbour this parasite. Foulerton [17] and, later, Stephenson and Balfour [18] found that no less than 22·6 per cent. of London rats are thus affected. Other wild animals can contract the infection as well. Our honorary secretary, Mr. George Dunkin [19], recently found a young fox naturally infected near the laboratory at Mill Hill. This disease may also possibly be conveyed to carnivora in captivity through eating infected rats. Apparently this recently occurred in the London Zoological Gardens, but since Dr. Vevers has forbidden the feeding of these animals with rats the disease has disappeared. Last year it was proved by Okell [20] and others that a naturally

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acquired typhoid-like illness known as epizootic jaundice in foxhounds is also due to the same parasite. To add to the interest of this subject it has been found that spirochaetes of the *Leptospira* type are widely distributed in water [21], especially that of contaminated wells and rivers, and that small outbreaks of Weil's disease have recently been reported in man from Scotland (East Lothian and Edinburgh) and the Midlands. The probability is that this disease is normally conveyed by infected water contaminated by rats, which constitute the reservoir host of the disease. It is a matter of considerable interest, and a subject for speculation, as to why the closely related *Leptospira icteroides*, the organism of yellow fever, should appear to be a parasite of man only. Arguing by analogy from what we know of Weil's disease, which yellow fever so closely resembles in its clinical course, one would surmise that this organism was widely distributed amongst monkeys and other small mammals in those countries (South America and West Africa) in which yellow fever is endemic. The reservoir host, if other than man himself, has still to be discovered.

There still remains to be mentioned a leptospiral disease which has recently been described. This is the seven-day fever of the Japanese. The organism was first discovered in 1918 [22] by Ido, Ito, and Wani and named *Leptospira hebdomadis*; it is apparently a parasite, like *Leptospira icterohæmorrhagiae*, of the urinary tract of the common field vole, *Microtus montebelloi*, Milne-Edwards. Very little is known about the fever in man, except that it lasts seven days and does not appear to be a fatal disease.

The *Microtus* [23], wrongly called in text-books a field mouse, is really a stump-tailed vole, which is common in country districts in Japan, and is closely allied to similar voles which occur in China and Tibet. There is little to be said about its habits, except that it burrows and feeds upon roots and grain in much the same manner as do similar creatures in other countries.

RAT-BITE FEVER.

This is a world-wide disease, but it appears to be specially common in Japan.

Following on the bite of an infected rat, sometimes after a prolonged incubation period, a lymphangitis supervenes which implicates the glands of the area involved. Then follow many short attacks of fever coinciding with an exacerbation of local symptoms.

The organism, *Spirillum minus*, was formerly thought to be a spirochaete, is very minute, $1.5\ \mu$ to $6\ \mu$ in length, and can be found in the blood, as well as in the lymphatic glands, during the height of the disease. This fever is transmitted by the brown rat (*Rattus rattus* and *Rattus alexandrinus*), and the organism is probably identical with *Spirillum laverani* and with *Spirillum muris*, which are commonly found in the blood of rats and mice. It is said that the disease can also be conveyed by the bite of a ferret or by that of the domestic cat. The wild cat has also been incriminated. *Felis catus*, Linn. [24], is said to still exist in the Highlands of Scotland in a purely wild state, but this statement is doubted by many authorities, as it appears to have intermingled with the house cat wherever that familiar animal has penetrated.

ROCKY MOUNTAIN SPOTTED FEVER.

This is not a disease of the tropics at all; it is, however, peculiarly associated with the presence of wild animals. A typhus-like disease with a high mortality rate has long been known as "spotted fever," "blue disease," and "black fever"; and to be endemic in limited districts of Montana and Idaho and Wyoming. It has also been reported from the States of Utah, Nevada, Oregon, Colorado, and Washington. This fever is virulent, especially in the spring months of the year in the district of Montana known as the Bitter Root Valley. The causative organism belongs to that

rather nebulous group, the *Rickettsia*, and is known as *Dermacentor rickettsi* [25]. It is conveyed by the bite of a tick peculiar to that region, known as *Dermacentor venustus*. It is only the adult tick that attacks man, but it commonly infests the Rocky Mountain goat, the badger, lynx, bear, coyote, and other animals that inhabit that region. The larval and nymphal stages of the tick develop principally on the ground squirrel (*Citellus columbianus*) and the woodchuck (*Marmota flaviventris* nosophora, Howell). The last two rodents are considered to be the main reservoir hosts of the *Rickettsia* and, although a certain proportion are capable of infection in the laboratory, it is thought that they may develop the disease in a mild form under natural conditions. Of the larger animals the tick most favours the Rocky Mountain goat (*Oreamnus montanus*) [26]. It is not really a goat at all, but is most nearly allied to the serows, a rare animal at the present day, as it only exists where strictly preserved. The American badger (*Taxidea taxus*) resembles its European relative, with the difference that its diet is more carnivorous. The black bear (*Ursus americanus*), and the lynx (*Lynx uinta*) hardly call for comment. The coyote (*Canis latrans*, Say) is a small slinking wolf-like creature which differs from its European congeners in living in burrows in the plains.

The Columbian ground squirrel (*Citellus columbianus*, Ord) [27] is closely allied to the chipmunk, and is an intelligent little creature like its near relative; it lives amongst the birchwoods, where it digs its burrows in such a manner as to avoid attracting the attention of its enemies. In order to do so it removes the earth in its cheek pouches and carries it to a considerable distance. In winter the ground squirrel hibernates and in this state it probably harbours the virus of Rocky Mountain fever, so that it is able to convey the disease shortly after its spring awakening.

The woodchuck (*Marmota flaviventris*) is really a marmot, about 2 ft. in length; it is a thick-set creature with short legs and a stout bushy tail. It is grizzly or yellowish-grey in colour and hibernates all the winter long. Being vegetarian in diet, it lives in woodlands, never in the open plains, and is said to be the least industrious of all animals, to show energy only when digging its burrows, which may be 50 ft. or more in length.

PLAGUE.

Plague is essentially in the first place a disease of rodents and not of man. As Macarthur has so lucidly pointed out recently, much suffering would have been saved in the City of London had this been recognized in the Middle Ages.

Although the rat is the main reservoir of plague, many other rodents in many other parts of the world play a not inconsiderable part.

There are, as is well known [28], two species of domestic rat, of which the black rat (*Rattus rattus* Linn.) is the more important in the spread of the disease. The old English rat, as it is called, is rapidly vanishing from this country, being ousted by the more virile North European species (*Rattus norvegicus*, Berkenhout), which was apparently imported into Western Europe in the year 1716 as a result of a visit by the Russian Fleet. The black rat in India, in Burma, and in fact in the tropics generally, lives more closely in association with man; it is essentially an arboreal or climbing animal and rarely burrows; hence, when it infests buildings or huts, it is found usually in the walls, ceilings or roof. It drinks little and seldom enters the water voluntarily and it is the common rat on ships. In most cases it reaches or leaves the ships by clambering along the cables whilst the ships are in dock. Its dietary consists mostly of grain, and it is a much cleaner feeder than *Rattus norvegicus*. In appearance it differs also from *norvegicus* in its more slender build and large transparent ears. The weight of the adult is 8 oz.

There are several races of *Rattus rattus* which have been distinguished. One variety with reddish-black and pure white underparts is known as *Rattus rattus frugivorus* and is common in the Mediterranean area. The Alexandrine rat (*Rattus*

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rattus alexandrinus), with brownish-grey back and dingy coloured abdomen, is found in Asia Minor and North Africa. *Rattus rattus rufescens* is the common Indian house rat and is distinguished by its smaller size, its long tail and the spinous hairs with rusty tips on its abdomen. These rats breed throughout the year, gestation lasting twenty-one days, the average litter being five or six.

The brown rat (*Rattus norvegicus*) is distinguished by its larger size, its heavier and clumsier build and by its blunter muzzle. The ears are small and opaque; the tail noticeably shorter than the head and the body. The weight of the adult is about 17 oz. This rat is now developing a melanistic or black variety which was originally described in Ireland. Its home was originally temperate Asia. It is a water-loving and burrowing animal and is consequently far less agile than the former species, but it is far more voracious and cunning and is possessed of greater strength and fecundity. Usually exhibiting a shyness of man it is under normal conditions a less important carrier of plague than is *Rattus rattus*. *Rattus norvegicus* is a very rapid breeder, the litter varying from six to twenty-three, the average from eight to ten.

In various parts of the world other rodents are capable of replacing the rat in the spread of plague. In California, McCoy has shown that the Californian ground squirrel plays an important part, and that the plague bacillus is transferred by the flea (*Ceratophyllus acutus*) to rats and so to man. This ground squirrel (*Citellus grammurus beecheyi*, Richardson) [29] is in reality a spermophile and lives in burrows. In Southern Russia and the Caucasus other ground-squirrels (*Citellus*) are said to carry plague. These rodents are really a connecting link between the squirrels and the marmots. They are generally to be found in prairie-like regions, where they form an intricate system of burrows, at the mouth of which they are commonly to be seen standing upright and motionless. The common European species is *Citellus citellus* Linn., and is known in Russia as the "suslik." In Mongolia a subspecies known as *Citellus dauricus* plays a similar part. These animals hibernate throughout the winter and are responsible for the summer outbreaks of pneumonic plague in Mongolia and Manchuria. In these regions, too, the common house mouse, *Mus musculus*, is held to be responsible for winter outbreaks of plague, though it does not appear to play a dominant part in other regions. In North China, Siberia and Manchuria the Mongolian marmot or "tarabagan" (sometimes called tarbagan, or sarabagan (*Marmota bobak*, Müller) [30] has been held to be responsible for many serious outbreaks of pneumonic plague. These marmots are of a large size and strong build. They are characterized by the rudimentary character of the thumb, their small eyes and ears; the tail is bushy and comparatively short. In length (exclusive of tail) they are 15 to 18 in., and 9 to 12 lb. in weight. They make large, deep and intricate burrows where they hibernate. The mounds of earth thrown up by generations of tarabagans are known as "bootans," and are characteristic of the region they inhabit [31]. The flesh of the tarabagan is eaten by the Mongols, or "Buriats," and its fur is in much demand, being sold after drying and curing as imitation sable or seal [32]. This creature is credited with the faculty of harbouring the plague bacillus in its body during hibernation, and thereby causing outbreaks of pneumonic plague amongst the hunters, who live under miserable conditions huddled together in underground hovels during the autumn and winter. The "Buriats" are said to be well aware of the danger of handling sick tarabagans, the infected animals being recognized by ceasing to bark and by being ejected by their healthy companions when they attempt to crawl back into their burrows.

In India, besides the rat, an insectivore, the musk shrew, *Pachyura cærulea* [33], plays a part in conveying plague. This shrew is about 6 in. in length, with a tail of 3½ to 4 in. It is coloured uniformly with a bluish-ash or pale grey hue, slightly tinged with red, the naked parts being flesh coloured. Commonly called the "musk rat," it frequents houses at night time, running about the rooms hunting for cockroaches or other insects, and uttering, while so doing, a sharp, shrill cry. It is popularly

believed in India that the musky odour emitted by this shrew possesses such volatile and penetrating powers that it will actually permeate the cork of a bottle and taint the fluid within.

The bandicoot rat (*Bandicota gigantea* [34]) is also susceptible to plague. This is a large rat 15 in. in length, with a tail of 13 in. and weighing about 3 lb. when fully adult. The incisor teeth are peculiar, being olive green at their base and yellow at their extremities. It is a well-known rat throughout India and Ceylon; being of a large size it shows fight when cornered and grunts like a pig. Where European gardens are cultivated, as in Newera Eliya, Ceylon, it causes considerable damage amongst the potatoes and peas.

In South Africa, plague [35] [36] [37] has spread amongst a number of rodents. When first introduced in 1901 it was apparently confined to the domestic rats. Further outbreaks in 1903, 1914 and 1918, led to the suspicion that other rodents were concerned. Some of them are responsible, as is the Cape hare, for transmitting the infection over a considerable area, but the chief part is played by small rat-like animals known as the gerbilles; of these there are numerous species in South Africa.

The first is known as Lobengula's gerbille, *Taterona lobengulæ* [38]. Gerbilles are distributed all over South Africa south of the Sahara. They are all very closely related and are probably equally susceptible to plague. This particular species has been singled out by the health authorities in South Africa. It receives its specific name because it inhabits the former territory of Lobengula, the Matabele king. It is about 5½ in. from the nose to the root of the tail, the latter being 1 in. longer than the body. The fur is light fawn on the back, finely grizzled with dull black; the sides are pale fawn, the under parts are white and strongly demarcated. Although a gerbille, this particular species has the habit and structure of a rat. Other species probably involved are known as the Cape gerbille (*Taterona afra*) and Brant's gerbille (*Taterona brantsi*).

The white-nosed rat (*Rattus coucha*), sometimes called the multimammate mouse, is in appearance something between a rat and a mouse, and living in close association with the gerbilles, it is also frequently attacked by plague. This species is distributed throughout South Africa, and its range extends beyond the Equator to the Sahara. It is found in situations which afford abundance of cover, such as thick scrub. It is a house dweller and is often trapped in buildings and outhouses. The tip of its nose, as its name indicates, is white.

The Springhaas, or Cape jumping hare (*Pedetes caffer*), is a much larger animal, the size of a rabbit, and by far the largest of the jerboa family. It is common throughout the Cape Province. It is sociable in its habits and forms an intricate series of burrows in which a good many families take up their abode. When alarmed and travelling at full speed, it races like a kangaroo, each leap covering 8 or 9 ft. It is nocturnal in its habits and multiplies very rapidly. It has many natural enemies and is preyed upon by the Cape eagle owl. This species can travel 20 to 40 miles in a single night; on this account it is of importance in the spread of plague.

Carnivores which prey on these rodents, especially when sick, such as the yellow mongoose (*Cynictus penicillata*) and the suricat (*Suricator suricator*), are also found to die of plague; when the faeces contain the remains of gerbilles, which they feed upon only when they are sick, it is taken by the health authorities as an indication that plague is endemic in that particular area.

In Senegal and West Africa a shrew (*Crocidura stampflii* [39]) is said to play a part in the dissemination of plague. It lives in native houses and probably has much the same habits as those of the Indian musk rat and plays a similar rôle.

In England [40] the rabbit and hare were found naturally infected with plague in Suffolk in 1910.

TULARÆMIA.

Tularæmia is a plague-like disease which has been known since 1912 to affect jack-rabbits and other rodents, especially ground-squirrels, in California. Unfortunately it is communicable to man, in whom it causes an intractable illness.

Tularæmia [41] in man is a disease of the rural population, particularly in field workers, and is recorded amongst dealers who handle infected jack-rabbits. The organism, *Bacterium tularense*, is not easy to cultivate on artificial media: it is extraordinarily infective and many laboratory workers have contracted the disease. The infection is transmitted, from one infected jack-rabbit to another, by a blood-sucking fly, *Chrysops discalis*.

The jack-rabbit (*Lepus campestris*, Bachman) is a very familiar species in America. It is a large hare-like creature with long hind-legs and ears. In the northern parts of its range its coat turns white in winter, but further south this change is partial, or does not occur. Like our hare, it lives in the open and depends for safety on its protective coloration, speed and acute hearing. For its home the jack-rabbit has an open form beneath a bush or clump of weeds. Large numbers of these animals are killed annually in drives, as many as 20,000 having been accounted for in one day.

The ground-squirrel (*Citellus grammurus beecheyi*), which also forms a reservoir of infection, is the same species as that concerned in the spread of plague in California.

The gophers (*Geomyidæ*) form another source of infection. These are curious little animals, characterized by large cheek pouches opening outside the mouth, and they have feet with immense claws for digging. Their bodies are heavy and their movements slow and clumsy. Their habits are nocturnal and they live in communities in burrows. *Thomomys bottæ bottæ* (Eyndoux and Gervais), which extends along the coastal region of California, is the species concerned.

MELIOIDOSIS.

There still remains one more recently described glanders-like disease in man known as *Melioidosis* [42], which occurs in Burmah and the Malay States. The organism known as *Bacillus whittmori* occurs as a natural infection in the Malay rat (*Mus griseiventer*, Bonhote), which, in spite of its name, is the local representative of the common black *Rattus rattus*.

I have now summarized somewhat incompletely, I fear, the state of our knowledge regarding the wild animal reservoir hosts of human disease in the wilder portions of the earth. There still remains the helminthic infections that I do not propose to deal with in detail, but of which I append a list at the end of this paper.

There are other widespread and almost universal infections, such as malaria, in which the parasite, though indigenous in most parts of the tropics, is peculiar to man, and to man alone. Strange to relate, human malaria parasites have never been found in any other vertebrate host, not even in the larger apes which harbour, it is true, their own particular species of *Plasmodium*. From this circumstance I think we may fairly infer, from what we know of the natural history of other protozoal infections, that primæval man must have acquired his parasite from some reservoir host.

If it is usually considered permissible for ethnologists, dealing solely with his more durable remains, to speculate upon the heredity of man, so it is equally permissible for the parasitologist to speculate upon the probable evolution of man's diseases. It may be that the original reservoir host of malaria was some hoary and hairy simian anthropoid, one of the missing links long since extinct and whose bones lie buried deep in the alluvial earth of Central Africa. But though the anthropoid became extinct, his parasite did not and was transmitted as a sort of heirloom to his more intelligent and highly developed descendant—man.

But whence did these remarkable parasites arise, organisms which have such an intricate life-history? Did the malaria parasite first exist in the mosquito and later in man, or vice versa? Were the trypanosome and tsetse on intimate terms long before man was swinging in the tree tops of the great African forest? I fear that we have no very exact data upon which to base any reasonable hypotheses. One can readily understand how a free-living organism can readily adapt itself to the life of another animal (there are plenty of instances of this in Nature), but it is more difficult to explain how it can accustom itself to hosts so entirely dissimilar in structure and habits, as man and the tsetse, or man and the mosquito, and as to how the parasite came to lead the entirely different life-cycles within the vertebrate and invertebrate host.

Possibly the blood protozoa of man and animals were at one period parasitic in the latex of certain plants, and, through being constantly ingested by insects which feed on these juices, they eventually came to adapt themselves to a semi-parasitic existence within the alimentary canal of the insects. In course of time, and in process of evolution, the predatory instincts of a more adventurous bug led it to feed upon the warm blood juices of rodents and other mammals. Ingrained habits may change; thus the Kea parrot of New Zealand (*Nestor notabilis*) found the liver of sheep imported into that country more succulent than the acrid fungi upon which it was wont to feed. It may be so, by constant close association of insect with food supply, that the primitive parasite followed suit and came to pass part of its existence first in the one and then in the other.

Certain discoveries which have been made in recent years support this hypothesis.

Flagellates of the *Leptomonas* type, closely allied to leishmania, have been found by Lafont, Migone (1916), França (1921), and others, in the latex of plants of the genus *Euphorbia*; the second named observer has shown that a plant bug, *Stephanoccephalus agilis*, is responsible for the spread of infection from plant to plant in Portugal. The bug, which is nocturnal in its habits, punctures, while feeding, the leaf of the plant in many places and transmits the parasites through its salivary glands. Strong (1924) makes a stronger claim in stating that lizards which devour certain of these plant bugs acquire an intestinal infection with the flagellate, which then, he asserts, assumes pathogenic properties for monkeys.

Other flagellates which they closely resemble in structure inhabit the intestinal tract of house flies (*Herpetomonas muscae domesticæ*), bluebottles and even biting flies.

From a morphological standpoint these free-living forms are indistinguishable from the evolutionary stages of trypanosomes and leishmania, the familiar blood protozoa of man.

It has been further claimed by some investigators, notably Laveran, Franchini, and Fantham, that vertebrates, particularly mice, may be easily infected with insect flagellates by inoculation or feeding, and that in some instances a diseased condition resembling kala-azar may result. But this work has not received the necessary confirmation, so that it is only by intensive research and numerous transmission experiments with these lowly forms of life that further light can be shed, not only on the origin of the parasites themselves, but also upon the chequered history of *Homo sapiens* himself.

I must acknowledge, as is only due, my gratitude for the generous assistance I have received in preparing this paper from Mr. M. A. C. Hinton, of the British Museum, Mr. Martin Duncan, of the Zoological Society, and Dr. Daukes, of the Wellcome Bureau.

LIST OF HELMINTHIC PARASITES FOUND IN MAN AND WILD ANIMALS.

TREMATODA:—

Fasciola hepatica. Wild ruminants, deer and antelopes.

Heterophyes heterophyes. *Canis nilotus*. Egypt.

42 Manson-Bahr: *Relationship of Wild Animals to Diseases in Man*

TREMATODA (continued).

- Paragonimus westermanii*. Tiger and leopard. India.
Schistosoma hæmatobium. Sooty mangabey monkey (*Cercocebus fuliginosus*).
Schistosoma japonicum. Rats (*Rattus*). China.
Gastrodiscoides hominis. Mouse-deer (*Tragulus napu*). Malay States.

CESTODA :—

- Cysticercus cellulosæ*, larval stage of *Tænia solium*. Wild boar (*Sus scrofa*).
Cysticercus bovis, larval stage of *Tænia saginata*. Giraffe (*Giraffa camelopardalis*).
Hymenolepis diminuta. Rats (*Rattus rattus*, *Rattus decumanus* and *Rattus alexandrinus*). Mice (*Mus musculus* and *Mus sylvaticus*).
Dipylidium caninum. Jackal (*Canis aureus*).
Echinococcus granulosus, larval stage of *Tænia echinococcus*. Wolf (*Canis lupus*).
 Jackal (*Canis aureus*).
Sparganum mansoni, the plerocercoid stage of *Dibothriocephalus mansoni*. Frog (*Rana nigromaculata*). Snakes (*Elaphe climacophora*). Japan.
Diplogonoporus grandis. Various species of seal. Japan.

NEMATODA :—

- Belascaris canis*. Fox (*Canis vulpes*).
Torascaris canis. Wild cat (*Felis catus*).
Ternidius deminutus. Monkeys (*Macacus sinicus* and *Macacus cynomolgus*).
 Nyasaland and Transvaal.
Physaloptera mordens. (*Macacus sinicus*) Nyasaland.
Ancylostoma duodenale. Tiger. India.
Ancylostoma ceylanicum. Civet cat (*Viverricula malaccensis*). Ceylon. Clouded leopard (*Felis nebulosa*). Malay States.
Necator americanus. Gorilla (*Gorilla savagei*). Patas monkey (*Cercopithecus ruber*).
Esophagostomum apistomum. Gorilla. Orang-outang (*Simia satyrus*).
Trichuris trichiura. Various old-world monkeys.
Hepaticola hepatica. Rat (*Rattus norvegicus*).
Trichinella spiralis. Wild boar (*Sus scrofa*).
Loa loa. Baboon (*Papio cynocephalus*). West Africa.
Acanthocheilonema perstans. Chimpanzee (*Anthropopithecus troglodytes*). West Africa.
Dracunculus medinensis. Jackal and leopard.
Gnathostoma spinigerum. Tiger. India. Puma (*Felis concolor*). South America.

REFERENCES.

- [1] ROTHSCHILD, W., *Nov. Zool.*, 1890, v, p. 206. [2] SCLATER, P. L., and THOMAS, "The Book of the Antelope," 1899-1900, iv, No. 151-160. [3] DUKE, H. L., "Reports of Sleeping Sickness Commission," 1913, *Roy. Soc.*, No. 13, pp. 54-57. [4] *Idem*, *Journ. Trop. Med. and Hyg.*, 1915, xviii, No. 2, pp. 13-16. [5] WECK, *Arch. f. Schiffs. und Tropenhyg.*, xviii, pp. 113-124. [6] "The Book of the Antelope," 1896-97, ii, pp. 97-103. [7] *Idem*, pp. 157-164. [8] *Idem*, 1894-1900, i, pp. 203-211. [9] BRUMPT, E., "Nouveau Traité de Médecine," Fasc. v. [10] GODWIN and SALVIN, "Mammalia," *Biol. Central. Amer.*, 1879-1882, pp. 188-190. [11] BEDDARD, F. E., "Mammalia," *Camb. Nat. Hist.*, 1903, p. 178. [12] GODWIN and SALVIN, "Mammalia," *Biol. Central. Amer.*, pp. 197-198. [13] WATERHOUSE, G. R., "A Natural History of the Mammalia," 1848, ii, pp. 164-168. [14] SMYLY, H. J., and YOUNG, C. W., *Proc. Soc. Exper. Biol. and Med.*, 1924, xxi, No. 6, pp. 354-356. [15] MILNE-EDWARDS, M. A., *Rech. p. servir l'Hist. Nat. d. Mamm.*, 1868-1874, pp. 133-135. [16] INADA, R., IDO, Y., KOHI, R., and ITO, H., *Journ. Exper. Med.*, 1916, xxiii, p. 377. [17] FOULERTON, A. G. R., *Journ. Path. and Bact.*, 1919, xxiii, No. 1, p. 78. [18] BALFOUR, A., *Parasitology*, 1922, xiv, Nos. 3 and 4, pp. 282-297. [19] *Rep. Med. Res. Comm.*, 1924-1925, p. 31. [20] OKELL, C., DALLING, T., and PUGH, L. P., *Vet. Journ.*, 1925, lxxxi, No. 1, pp. 3-35. [21] HINDLE, E., *Brit. Med. Journ.*, 1925, ii, pp. 57-59. [22] IDO, Y., ITO, H., and WANI, H., *Journ. Exper. Med.*, 1918, xxviii, No. 4, pp. 435-448. [23] MILNE-EDWARDS, M. A., *Rech. p. servir l'Hist. Nat. d. Mamm.*, i, pp. 284-286. [24] HAMILTON, E., "The Wild Cat of Europe," 1896, London, R. H. Porter. [25] WOLBACH, S. B., *Journ. Med. Res.*, 1919, xli, No. 1, pp. 1-197. [26] STONE, W., and CRAM, W. E., "American Animals," 1903. [27] MERRIAM, "North American Fauna," 1891, No. 5, p. 41. [28] HINTON, M. A. C., "Rats and Mice as Enemies of Mankind," *Brit. Mus. Nat. Hist. Series*, 1920. [29] MERRIAM, *Proc. Biol. Soc.*, Washington, 1893, viii, p. 133. [30] WU LIEN TEH, "North Manchurian Plague Prevention Service," 1911-1913, *Camb. Univ. Press*, 1914. [31] *Idem*, "North Manchurian Plague Prevention Service," Reports, 1918-1922. [32] PREBLE, P., "The

Tarabagan (*A. bobac*) and Plague," *Public Health Reports, U.S.A.*, 1912, No. 68. [33] JERDON, T. C., "The Mammals of India," 1874, pp. 53, 54. [34] "Plague," *Journ. of Hyg.*, No. 11, 1907, p. 760. [35] HAYDON, L. G., *Lancet*, 1921, ii, pp. 103-104. [36] MITCHELL, A., 1923 *Public Health Report (South Africa) for the Year ended June 30*; *ibid.*, 1924. [37] KAUNTZE, W. H., "Report on an Investigation into Plague in the Union of South Africa," *Kenya Med. Journ.*, 1925, ii, No. 11, pp. 163-182. [38] FITZSIMMONDS, F. W., *Nat. Hist. of South Africa*, 1920, Longmans, Green and Co., pp. 89-91. [39] LEGER, M., and BAURY, A., *C. R. Acad. Sci.*, 1922, clxxiv, No. 6, pp. 423-426. [40] MARTIN, C. J., ROWLANDS and BULSTRODE, "Observations on Rat Plague in East Suffolk, 1910," *Report of Local Government Board, 1910-1911*, p. 36. [41] FRANCIS, E., *Public Health Reports, U.S.A.*, 1921, xxxvi, No. 30, pp. 1731-1738. [42] STANTON, A. T., and FLETCHER, W., "Meloidosis, a Disease of Rodents, communicable to Man," *Lancet*, 1925, i, pp. 10-13.

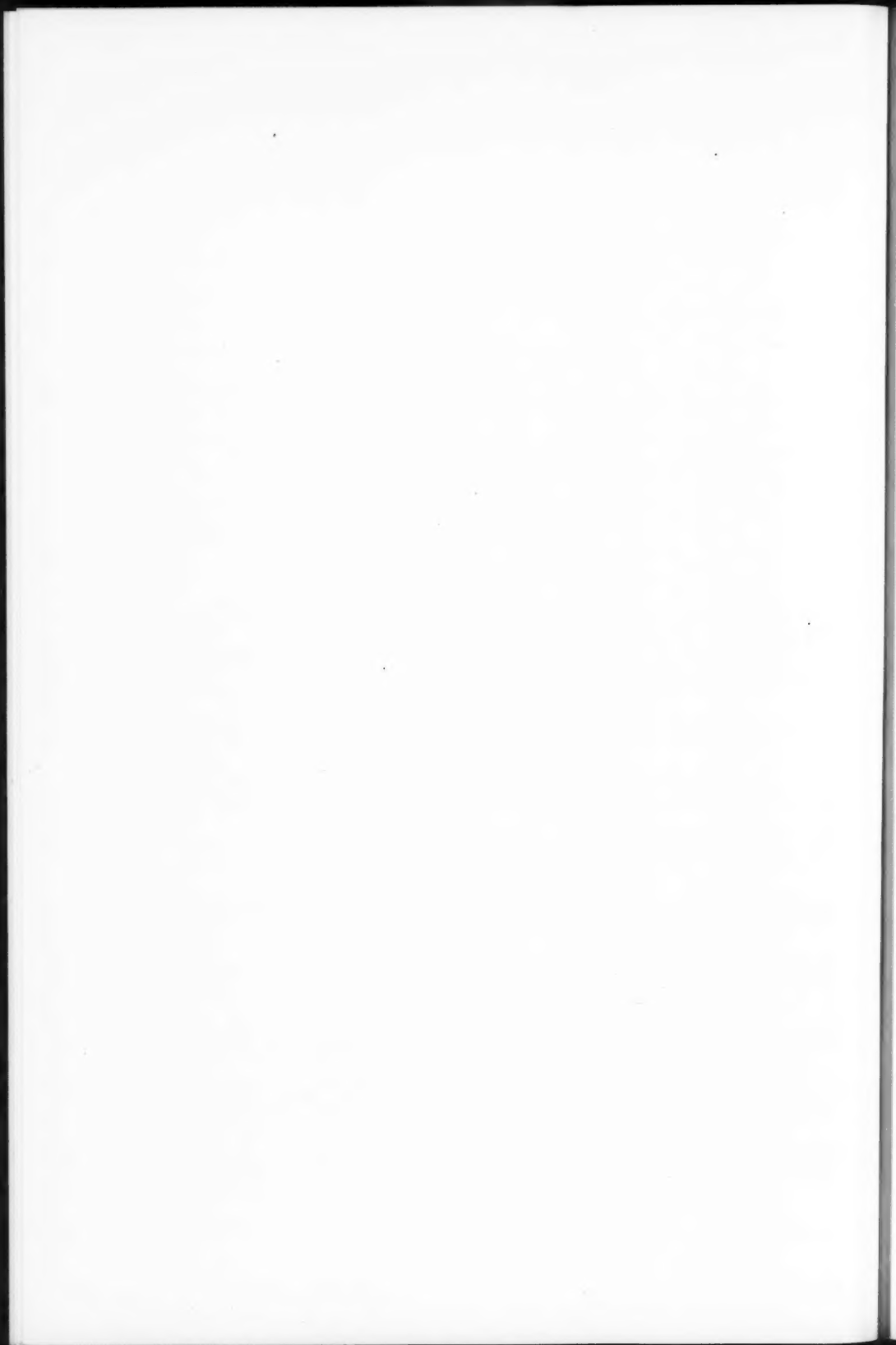
Discussion.—Dr. H. HAROLD SCOTT said he was a little surprised that such an important disease as rabies had not been mentioned, but naturally in a paper which had to be of limited length owing to time available, some omissions must be expected. He spoke of two interesting conditions which might, perhaps, be regarded more as common to man and animals than actually communicated from the latter to the former, though communication was quite possible. The first was a small epidemic he had investigated amongst the hamadryas baboons at the Zoological Gardens, in the course of which sixteen of them had died with intestinal ulceration. From twelve of these he isolated from the bile and from septicæmic abscesses in the lungs and the liver the *Bacillus aertrycke* which was the cause of severe and often fatal lesions in man. The second was the isolation of *Bacillus morgan*, No. 1, from two *Patas cercopithèques* recently dying from enteritis at the Gardens. This organism, as was well known, had been incriminated as one of the causes of summer diarrhœa of children—a disease commonly fatal.

(Communication to the Discussion made by letter dated January 19, 1926.)

Mr. EUSTACE MONTGOMERY (Nairobi, Kenya): I wish I could be present for Manson-Bahr's paper, but it is a combination, i.e., wild animals and man, of which I have no personal experience except our pseudo-rabies and trypanosomiasis. The former appears indeed not to be a "disease" of man and the latter could be discussed with advantage, but without finality, for days. What, however, might with advantage be brought out at the discussion is the great anomaly of "game" control in most of our tropical possessions. I am a keen "shikari" and advocate protection against extermination for many reasons, but as practised by a game "department," numbers and range of species are encouraged to expand, largely at the expense of man or his domestic stock. In such fortunate countries where there exist no diseases (contagious) of stock, and where grazing, water, &c., suffice for all, no harm is done. But in such as Eastern Africa, the veterinary departments, armed with very elaborate and often most penalizing "Diseases of Animals Ordinances," demand of a stock owner that he shall fence his land, brand his cattle, &c., inoculate them against various diseases and so on. In other words great restrictions are put on domestic mammalia in the interests and needs of disease control. In most countries, for example, no cattle can be taken from one village to another without a written permit specially obtained. Yet we encourage wild mammalia, lacking even the most primitive control of the most uncivilized natives' cattle, to roam at will without fences, permits, brands or inoculations. Wild and domestic are susceptible to the same great East African menace—rinderpest—and are naturally carriers and disseminators; and, without question, inquiry would disclose more than rabies, anthrax, swine fever, horse-sickness as between wild or domestic.

Both are susceptible mammals; oftentimes the wild is the greater menace, and yet for the sake of "protection," as well as revenue from licences to shoot, this extraordinary difference is made between the classes. Either the precautions now applied to the domestic are unnecessary or the freedom to the wild to roam and propagate is undesirable. In any case, it is illogical so to make fish and fowl of susceptible species of a common stock.

The remedy is not game destruction, as some would urge, but scientific game protection, as there is scientific stock protection, and this would also encourage inquiry into habits as well as diseases intercommunicable with man and domestic stock. We have many men ideally competent for such observation, and, if they do not want to be bothered to sell licences and to prosecute poachers, there are such departments as Revenue, Administration and Police quite well constituted for this everyday purpose.



Section of Comparative Medicine.

President—Mr. FREDERICK T. G. HOBDAY, C.M.G., F.R.C.V.S.

Ultra-violet Radiation in Man.

By J. F. HALLS DALLY, M.A., M.D.Cantab., M.R.C.P.Lond.

[ABSTRACT.]

THE nature and effects of ultra-violet radiation constitute a study of increasing practical importance, so that, in the interests of patients, whether human or lower animal, subjected to this form of radiant energy, it behoves us to proceed with caution, and to analyse with the greatest care the principles upon which this method of treatment rests.

Let us at once frankly admit that such principles are still based on slender supports. What little we do know is mainly due on the part of applied science to the well-known observations of Professor Leonard Hill and of his co-workers in this country, as well as to Professor Carl Sonne and his well-known predecessors, Finsen, Reyn, Ernst and others of the Danish school. On the clinical side, Sir Henry Gauvain, Dr. Howard Humphris, Dr. Kerr Russell, Dr. Percy Hall, and others in this country, have published the results of their practical experience, while abroad useful references are to be found in American, French and German literature.

THE RELATIVE POSITION OF ULTRA-VIOLET RAYS IN THE ELECTROMAGNETIC SPECTRUM.

The electromagnetic spectrum is composed of a continuous series of eighty known octaves of radiant energy, invisible and visible, classified according to wave length and frequency. Wave length is the distance between any two corresponding points on successive waves in the direction of propagation, and is commonly measured in terms either of the Angström unit (A.U.), whose length is one ten-millionth of a millimetre, or of the micron (μ), one thousandth of a millimetre. Frequency is calculated by dividing velocity of transmission by wave length. Thus, since all electromagnetic waves travel through a vacuum with a uniform velocity of 186,300 miles per second, the shorter the wave length the more rapid is the frequency of the periodic vibration of its electrons.

Starting at the zero end of the spectrum, a progressive increase of wave length takes place from the shortest known rays recently discovered by Millikan, through the very short gamma rays emitted by radium, onward through X-rays to the five octaves of ultra-violet. These are divided into extreme (with which we are not directly concerned), middle (2,000-3,000 A.U.), and near ultra-violet rays (3,000-3,900). Then follow luminous rays (3,900-7,700). If we repeat Newton's original experiment (1666), and pass through a prism a beam of white light, it becomes diffracted into its characteristic violet, indigo, blue, green, yellow, orange and red primary rays. Hence, transferring to its appropriate place in the electromagnetic spectrum this visible colour band, we find that it occupies only one octave, or one eightieth part of the sum-total of radiant energy. These luminous rays are succeeded by infra-red or heat rays, and passing further through Hertzian waves, the longer of which are used in wireless, we find at the opposite end of the spectrum the longest wave lengths of slow oscillation. Luckiesh states that if visible light be represented by one foot, the entire spectrum would extend several million miles in length.

TYPES OF LAMP EMPLOYED TO PRODUCE ULTRA-VIOLET ENERGY.

These fall into three main types : (I) The Carbon Arc ; (II) The Quartz-Mercury Arc, (III) The Tungsten Arc.

COMPARISON OF EFFECTS PRODUCED BY THE THREE TYPES OF ULTRA-VIOLET LAMP.

Comparison of the spectra shows that the tungsten arc affords the greatest amount of short ultra-violet rays, the mercury arc being intermediate in action with a discontinuous spectrum containing more of the middle ultra-violet rays, whilst the cored-carbon arc yields a continuous and even radiation approximating closely to that of the solar spectrum.

For biological irradiation I prefer the carbon arc, and in private practice I use the quadruple arc with core carbons, having solid cores of boron, calcium, magnesium, and aluminium in descending order, which gives very uniform and satisfactory results. With Professor Sonne I hold that these biological effects are not solely a question of ultra-violet energy, but that the luminous rays "possess a faculty of heating to a high degree the sanguiferous layers of the skin and of the underlying tissues, and that this heating is a factor of great importance." Incidentally, heat production serves as a guide to dosage, for, if the patient's skin begins to feel uncomfortably warm, treatment can be stopped at the point of inducing erythema, which constitutes the biological dosage usually to be aimed at, in order to raise the immunizing power of the tissues.

Clinical evidence in support of these views is derived from the extremely good results which follow the use of the carbon arc and outweigh the therapeutic effects attained from the use of "cold" lamps, such as the mercury-vapour and tungsten arcs. In fact, many workers have more or less unwittingly reached this conclusion by employing the Sollux or other forms of luminous heating preceding the use of the "cold" lamp, or two carbon arcs in combination with a quartz-mercury arc, and have thereby secured better results.

BIOLOGICAL EFFECTS OF ULTRA-VIOLET, LUMINOUS AND INFRA-RED RAYS.

Depth of penetration varies directly with increasing wave length down to the red end of the luminous spectrum, and with intensity of radiation which varies as the square of distance from the source.

2,400 A.U. represents the threshold of penetration. Rays shorter than this are absorbed by the oxygen of the air. The lower half of the middle ultra-violet series becomes correspondingly more active as the wave lengths increase from 2,400 to 3,000 A.U., the most potent being close to 3,000 A.U. These, however, penetrate only from 80 to 130 microns. The middle rays presumably get through the horny layer of the epidermis in which they are wholly absorbed, whilst the near ones reach the blood-capillary layer. Luminous rays, according to Professor Leonard Hill, go deeper and are absorbed in blood, muscles and joints, whereas the infra-red rays apparently get no further than the superficial skin layers. Rays must be absorbed in order to become effective, and in this process electrochemical and other changes are set up.

GERMICIDAL PROPERTIES OF ULTRA-VIOLET RAYS.

Wave lengths shorter than 2,800 A.U. appear to have abiotic properties, and to be lethal to many organisms and bacteria, but their uses are limited, since they penetrate only about 2 microns of tissue. Relatively deep sterilization may be effected by staining the tissue cells with fluorescent dyes, or by injecting these. Increased lymphocytosis results from wave lengths longer than 2,800 A.U. Dr.

Colebrook, Dr. L. Hill, and Dr. Eidinow¹ believe that the germicidal powers of the blood are enhanced by partial systemic doses sufficient to produce erythema from five to ten minutes twice a week, and that longer exposures lessen this effect, since the skin has the power of immunizing itself against these rays, with resultant thickening of the horny layer by reason of the inflammatory reaction set up. Many further investigations on hæmobactericidal power, however, are necessary before any really absolute conclusions as to this can be reached.

ANALGESIC PROPERTIES OF ULTRA-VIOLET RAYS.

Research is urgently needed as to the anæsthetic and analgesic properties of ultra-violet rays, since these may ultimately prove to be of considerable practical importance. It is certain that they relieve pain, whether of superficial areas or deeper viscera, though we do not understand the mechanisms involved. It may be that superficial pain sensations are allayed by direct action on interepithelial nerve fibrils, and that visceral pains are favourably influenced by lessening of internal congestion through derivation of blood to the surface capillaries, or by irradiation of the cerebro-spinal nervous system, but all these are mere conjectures.

EFFECTS OF ULTRA-VIOLET RAYS UPON METABOLISM.

(1) Protein Metabolism.

It is probable that ultra-violet energy does not influence metabolism in general, but only special kinds, particularly protein metabolism as measured by the urinary nitrogenous metabolism which is increased. Recently, whilst in Switzerland, I was told by Professor Loewy that animals and human beings sensitized by injections of dyes exhibit qualitative changes in protein metabolism, the percentage of ammonia being increased from a normal 4 per cent. up to 6 or even 8 per cent.

(2) Mineral Metabolism.

(a) *Calcium Metabolism.*—Subsequent to irradiation the absolute amount of calcium increases in the blood with a relative decrease of the potash, whilst in the urine, potash increases relatively to the calcium. The deeper internal action of ultra-violet rays, whether associated with luminous rays or no, is probably exercised directly upon the glands of internal secretion. Deficient calcium metabolism is connected in a certain group of cases with deficient parathyroid secretion. Systemic irradiation increases the amount of parathyroid parenchyma, with resultant increase of parathyroid secretion. In this regard the experiments of Grant and Gates² are of considerable importance. These observers irradiated normal clipped rabbits daily for thirty minutes at one metre from a quartz-mercury lamp during three to seven weeks so as to produce pronounced erythema and desquamation, followed by moderate pigmentation. Changes in absorption and excretion of calcium and in the calcium level of the blood took place, and the blood-calcium concentration rose to 12.9 mgm. per kilo. of body weight as compared with 11.9 mgm. in sixty control animals. At autopsy the parathyroid glands manifested relative increase of 32 per cent. above normal weights, the gland hypertrophy being due to a true parenchymatous hyperplasia.

Whether ultra-violet energy acts primarily on calcium absorption and excretion—so causing a rise of blood-calcium which results in parathyroid hypertrophy—or whether the primary action is upon the glands themselves, remains to be determined. In any event, these experiments form an additional link in the chain which unites the parathyroid glands with calcium metabolism.

(b) *Iron Metabolism.*—This responds as quickly and as surely to ultra-violet

¹ Colebrook, L., Eidinow, A., and Hill, L., *Journ. Exp. Path.*, 1924, v, p. 54.

² Grant, J. H. B., and Gates, F. L., *Proc. Soc. Exp. Biol. and Med.*, 1924, xxi, No. 5.

radiation as do rickets, tetany, and other such diseases associated with calcium deficiency. By changes primarily induced in the bone-marrow, excess or deficiency of red blood-cells and of hæmoglobin is alike balanced. Levy¹ found that mice artificially rendered anæmic showed improvement in the condition of the bone-marrow and spleen after irradiation, whilst similar effects have been demonstrated by Combe² in cases of intestinal auto-intoxication in man. In this way are explained the results obtained in chlorosis, which are brilliant, as well as the improvement in secondary anæmias and in the opposite condition of erythræmia, where, in a man aged 62, Lorand found a fall in the red-cell count from $7\frac{1}{2}$ million to $5\frac{1}{2}$ million after seven weeks' treatment, along with the return to normal size of the previously enlarged spleen and liver.

(c) *Phosphorus and Iodine Metabolism.*—Here the results are not so striking as in the case of calcium. In the blood the absolute amount of inorganic phosphates shows increase. The thyroid gland manifests greater iodine content, and hypothyroidic conditions are benefited. A balancing action in the opposite direction is observed in hyperthyroidism.

(d) *Regulation of Oxidative Functions and of Internal Secretions.*—Restoration of metabolic balance may further be instanced by the influence exerted by ultra-violet energy on conditions such as endogenous obesity and diabetes, where cases which are at a standstill become powerfully activated towards return to normal weight. Myxœdematous infiltration lessens and neurasthenias steadily improve. Other processes of suboxidation often associated with nervous manifestations, such as the rheumatic diathesis, are benefited. Old age and premature senility, with their attendant atrophic phenomena, such as falling out of the hair, are both suboxidative conditions allied with degeneration of all the ductless glands, and in these latter, as well as in obesity, ultra-violet radiation, when combined with administration of glandular extracts and iodine, gives excellent results in a short time. This combination is synergic, acting in a similar way upon general metabolism; it powerfully augments oxidation, promotes organic combustions, activates mineral metabolism, increases blood-formation and circulation, and aids the functions of the nervous system. Thus, by acting as sensitizers, glandular extracts intensify the deeper actions of ultra-violet rays.

(e) *Elimination.*—A point to which apparently attention has not previously been drawn is the effect of ultra-violet energy upon the kidneys. Shortly after biological irradiation, micturition becomes more frequent and an increased quantity of urine is passed, with an increase in the total solid constituents. Old subjects with deficient elimination through renal inadequacy, and tendencies to acidosis and acidæmia, pass greater quantities of urine than usual, of high colour, with increased urates and other solids.

(f) *Assimilation.*—Errors of assimilation are rectified, with coincident improvement in anorexia and gastro-intestinal symptoms.

SELECTION OF CASES FOR TREATMENT.

In place of haphazard irradiation on the "hit-or-miss" principle, one can arrive at a closer idea as to suitability or not by (a) preliminary careful physical investigation, combined with (b) estimations of arterial pressure, particular attention being paid to the diastolic limit, (c) blood-counts, (d) tests of basal metabolism, (e) biochemical tests of blood and urine, and (f) erythema tests or other tests of dosage.

Biochemically, ultra-violet radiation, like sunlight, swings the acid-base equilibrium of the tissues towards acidity. The normal ratio of free to combined acid in the rest urine, as Dr. Henry Ellis³ has shown, is 1:2. If, in a disease such

¹ Levy, M., *Strahlentherapie*, 1924, Bd. xviii.

² Combe, "L'auto-intoxication Intestinale," Paris, 1908.

³ "Reaction in Relation to Disease," 1924, H. K. Lewis.

as pulmonary tuberculosis, this ratio nears equality, the body is reacting to the limits of its capability, and is already drawing heavily on its defensive mechanisms. An extra strain will lower resistance, and thus it would be unwise to expose such patient either to artificial or natural light. With a normal 1:2 ratio one is safe, and ratios greater than this benefit from ultra-violet rays proportionally to the increase in alkalinity.

CHEST DISEASES WHICH BENEFIT FROM ULTRA-VIOLET IRRADIATION.

More detailed discussion of the numerous maladies in which it is claimed that ultra-violet energy has proved successful I leave to succeeding speakers, and will only briefly touch upon one or two with which, as a physician concerned with chest diseases, I am brought most into contact. My experience is that early and moderate grades of pulmonary tuberculosis do well, as is explicable if one regards this disease from the metabolic standpoint of calcium deficiency, characterized by depression of the acid-base equilibrium in the direction of alkalinity, and often associated with assimilation errors. Contra-indications to ultra-violet therapy are (a) fever, with rapid breaking down of lung tissue, and (b) active toxæmia.

At Mount Vernon Hospital and in the out-patient department belonging to it, we have installed ultra-violet lamps of the three main types, and with these have obtained encouraging results in all forms of tuberculosis, certain types of asthma and bronchitis, pleurisy and other lung conditions. In most children with enlarged mediastinal and cervical tuberculous glands considerable diminution in size of these and of the extent of shadow at the lung roots is evident on comparison with X-rays before and after six to twelve weeks' treatment with the carbon arc. With the tungsten arc we have found general improvement, but much less effect upon the glands. Comparative radiograms (exhibited) taken by Dr. J. E. A. Lynham, of tuberculous disease of the left wrist in a woman, aged 36, previously treated by immobilization for several months without benefit, show complete healing to have taken place after twenty-three exposures to the tungsten arc. The patient has since been able freely to use the wrist and to do all her own housework, including the scrubbing of floors. Several of my cases of early exophthalmic goitre with the carbon arc have shown reduction in size of the thyroid gland, with amelioration of other symptoms.

Many diastolic and systolic arterial pressures are lowered by biological doses sufficient to produce slight erythema, and I regard this method as one of the best at our disposal for reduction of arterial pressures which are too high, and the raising of those which are too low. Subsequent dosage at intervals suffices to keep the pressures within standard limits. Hyperpiesia is more amenable to reduction than is hyperpiesis with renal involvement. Nevertheless, many of these latter cases do remarkably well, and in all cases exhibit marked general improvement.

When one speaks of ultra-violet therapeutic effects, till now it has only been possible to refer to the clinical results attained within one's own experience or that of others. By such procedure it is difficult to arrive at definite conclusions, by reason of the immense number of variables involved, and, although clinicians have succeeded in pointing out certain paths along which ultra-violet therapy is likely to lead to successful issues, the science of this subject is still lamentably incomplete. Probably the most important single effect produced by ultra-violet rays is that of oxidation.

The medical profession is eagerly awaiting the results of proved observations on the part of physicists, biochemists and physiologists working in collaboration. Some little has already been done, but much remains to be done. I would urge for consideration that, starting with standard electrodes, standard strengths of current, standard positions of subject at standard distances from the arc, and standard lengths of exposure, the effects of small groups of measured wave lengths at definite intensities of radiation should be carefully studied.

Within the limits of time at my disposal it is impossible to do more than touch the fringe of this interesting subject, and I have tried to concentrate on some aspects of it which appear to me either of practical importance or not to have received sufficient attention.

The Therapeutic Effects of Ultra-Violet Radiation and High-frequency Currents in Animals.

By E. MIDDLETON PERRY, C.B.E., F.R.C.V.S.

I WILL only state the experience I have gathered in treating a few cases by this method and note any point which I think would tend to differ from the application of the treatment to the human subject.

I use the quartz mercury vapour lamp, which has acted most satisfactorily, and seems to be the most suitable for our work. I chose the standard in preference to the hanging type, as it is convenient to use.

The treatment of our patients is more difficult than in the case of the human subject.

(1) *The Coat of the Animal*.—This mitigates largely against the use of the treatment, for the owner may object to the hair being clipped. In many cases I have therefore not clipped the hair but have rubbed it up to enable the rays to penetrate to the skin. The rays can be, and are, applied to the abdomen and thighs where the hair is less thick, but this cannot be so good as irradiating the back and chest.

(2) *The Great Variations in the Thickness of the Patients' Skins*.—These are so great that they must be taken into consideration individually when estimating the amount of exposure which is to be given. My experience has been that it is most difficult to get even the first degree of erythema on the back of a dog, except those of the delicate toy breeds; even twenty minutes' exposure at 12 in. failed to produce change visible to the naked eye on the skin of a Great Dane.

(3) *The Question of Keeping the Patient at a Certain Distance from the Lamp*.—Our patients are usually extraordinarily good, but naturally they get wearied by being held in one position for some ten minutes with their eyes bandaged or covered.

At present my experience is that great use can be made of ultra-violet radiation in certain cases that either fail to respond to the usual medicaments applied, or do so very tardily. Many which respond to the use of drugs or to surgical means appear to be cured more quickly by the rays, and it is undoubtedly a pleasant and clean way of treating some skin diseases. The results in rickets are the same as in man.

A 7 months old Airedale, whose front legs were bent, joints very enlarged and misshapen, improved to such an extent after twelve applications, covering a period of four weeks only, that the owner is now getting him ready for exhibition, and he certainly has a very fair chance of winning in a small show.

Such cases as moist eczema respond quickly, even two applications making a very marked change—this is also the case with indolent wounds and ulcers which seem to take on a healthy appearance almost immediately.

This is illustrated by the case of a cat which was suffering from one of those horrible, almost gangrenous wounds (about $2\frac{1}{2}$ in. long and $\frac{3}{4}$ in. broad) of the tail with which all the veterinary profession are well acquainted and know of the difficulty in healing them. After six applications of the rays the wound was quite healed.

There seems to be a great stimulus to the growth of the hair by this treatment and I think most of the patients I have treated have improved very markedly in the coat, this being probably due, of course, to the general improvement in health.

Several cases of pneumonia have been treated with most satisfactory results, also cases of catarrhal distemper.

I have tried this form of treatment in several cases of chorea and found marked

improvement, but again, the good result has been probably due to improvement in the general health more than to any alteration in the nerve centres; it would seem that ultra-violet radiation has a marked effect in tuning up the system.

A few applications after any debilitating disease seem to produce a wonderful effect on the patient and brings the case to a satisfactory conclusion.

With regard to follicular mange I regret that I have not had the success I had hoped for in its treatment by this method. I have tried it in several cases. The first few applications appeared to promise good results but subsequent exposures failed to bring about the hoped-for cure.

It is stated that the ultra-violet rays can kill bacteria in normal tissue to a depth of 1 millimetre in five minutes, but the rays are not penetrative enough to reach the follicular mange parasite, perhaps on account of the thickness of the skin; or is it that the parasites are surrounded by a protective covering of pus or other matter which is impermeable to the rays? or perhaps I have produced a protective covering of horny epithelium by too frequent irradiation. I should be glad of enlightenment on this point, and any suggestion how to overcome the difficulty. If this parasite could be reached it would be quickly destroyed by the rays; the question is, how to reach it.

HIGH-FREQUENCY TREATMENT AS APPLIED TO ANIMALS.

This treatment is quite distinct from ultra-violet radiation although it is often called the "violet ray" treatment by unscientific people. I believe various properties have been attributed to these rays, but these are now considered to be more theoretical than practical. We can therefore assume that high frequency treatment is the application of an electrical current alone. As the name implies, the alternations are of a very high frequency—"frequency" being the number of complete cycles occurring in one second of time, and as this, in some apparatus, is estimated in millions, it is appropriately named.

This high frequency renders the treatment eminently suitable for our patients, as the alternations are so rapid they do not stimulate the sensory nerves and consequently do not produce muscular contractions. These contractions disappear at a frequency of about 10,000; for this reason our patients do not object to the treatment in the least, providing the electrode is placed on the skin before the current is turned on; even if this is not done it is very rarely that any resentment is shown and no restraint other than just steadying the animal is needed.

Constitutional Effects of the Treatment.

These are derived through auto-condensation and auto-conduction. The current increases bodily heat, to which the beneficial effect of these currents is attributed.

A form of cellular massage is also considered to participate; this can be understood when one considers the negative and positive wave-like currents which are passing through the tissues.

However, the general constitutional effects, according to Eberhart, are classed as follows:—

- | | |
|------------------------------------|--|
| (1) Increased general metabolism. | (5) Increased secretions. |
| (2) " glandular activity | (6) " eliminations. |
| (3) " temperature and bodily heat. | (7) Lower blood-pressure when hypertension exists. |
| (4) " oxidation and hæmoglobin. | (8) Soothing to the nervous system. |

There are various forms of apparatus on the market and the primary current used is an alternating one, which can be obtained from most main supplies. It is applied to the patient by means of the electrodes already mentioned, which are made in various forms to suit every requirement.

52 Perry: *Therapeutic Effects of Ultra-violet Radiation in Animals*

Last month a report of twelve cases treated by this method was published in the *Veterinary Journal*: the following is a brief summary.

Eight cases of paralysis completely recovered; in one case of paralysis of the tongue there was great improvement when the owner left my neighbourhood.

One case of paralysis of the hind quarters, in which the animal was eventually destroyed on account of its age, viz., 14 years; it had, however, improved to such an extent that it could stand if put on its hind legs. In one case of chorea, that of a puppy quite unable to stand, the animal was eventually able to follow the owner about the house, but could not get upstairs; in one case of old standing opacity of the cornea this has been largely dispersed.

The following additional cases have since been treated:—

(1) Pekingese, with partial paralysis of the hind quarters; could get up, but only with considerable effort, would walk a few steps and then topple over; it was completely cured after seven applications and could run round my consulting room, which has a linoleum covered floor.

(2) Fox-terrier, with partial paralysis, is now quite cured after twelve applications.

(3) Alsatian, aged 7 months, completely paralysed hind quarters with loss of control of bowels and bladder following distemper. Has had six applications and can walk and just run, if steadied a little by holding the tail.

(4) Pekingese, aged 10 years, completely paralysed in the hind quarters, was able to stand and walk a few yards after six applications, and now after the eleventh application can run quite well but is still a little unsteady.

I am also trying two cases of amaurosis, both following distemper, but I am afraid I shall have to report failures. The owner of one of the dogs is satisfied that there is improvement in the sight but I cannot appreciate it. The iris in each case remains widely dilated and I cannot get movement by any means.

In addition to these particular cases I have mentioned there is evidence of a great beneficial effect on the animals generally, and many owners have specially remarked on the general improvement. Even after the first application the dog is brighter and better in himself, and after a few treatments the benefit is appreciable in the appearance of his coat. The current has a wonderful effect of breaking down old epithelium and producing in the skin a soft flaccid feeling which is so indicative of good health; the coat takes on fresh lustre, which is particularly appreciated in the long hair breeds.

Discussion.—Professor LEONARD HILL said that in his opinion, what any source of artificial ultra-violet rays could do was neither more nor less than what the high sun could do at the seaside, or in the clear country air, or in the Alps. What the sun would do, these artificial sources would do in seasons when the ultra-violet rays, and to a great extent the visible rays also, were cut off by the mist and cloud of our climate, not to speak of our industrial and domestic smoke-screen. A great deal of nonsense was being talked nowadays about different sources and methods of getting ultra-violet radiation. It did not signify much what the source was, whether mercury vapour or arc, or whether a plain carbon arc or one with a core of iron, magnesium, or tungsten. Results could be obtained from any of these different sources. One distinguished clinician had stated that nothing should be used except the short-flame carbon arc with direct current, giving a flame that never flickered. That dogmatic kind of statement was unwarranted. One could get equally good results with long-flame arcs, which, incidentally, were far more economical in cost. The intensity of ultra-violet radiation obtained depended upon the energy which was put through the arc. If the energy, say of a 200-volt current, were broken up into four poles instead of two, the same ultra-violet energy would not be forthcoming as from two in series. By careful management comparatively weak sources of ultra-violet radiation might furnish whatever was necessary, but, of course, such weak sources were time-wasting. It had to be borne in mind also that the skin rapidly immunized itself against the dose it was receiving. The horny layer thickened, the skin became oedematous, and penetration correspondingly difficult. The active region in the ultra-violet spectrum was from 3,200 to 2,400 A.U. Rays shorter than this lower limit would kill bacteria, infusoria, and so on, but would not penetrate the

horny layer of the epithelium. He had had his skin subjected for half an hour to ultra-violet radiation of a wave-length of 2,320—an intensity which would kill all infusoria in a drop of water in a minute or so—and no erythema was produced at all. A slight erythema was produced with a wave-length of 2,500, and the maximum erythema effect was in the region of 2,950—3,000. He went on to speak of the conclusions of the long investigation on rickets. By ultra-violet radiation stearyl could be activated so that in a minimal dose it would cure rickets. If 1 mgm. a day of the activated stearyl were given to the animal there would be no rickets. The activation was brought about by half-an-hour's exposure. This activated stearyl or cholesterol was vitamin D. Ultra-violet radiation, therefore, could produce a vitamin, and produced it, as physicists told them, by altering the energy of the atoms. When eaten by the animal this activated substance enabled it to absorb from its alimentary canal the minimal quantity of salts of phosphorus and salts of lime which was deficient in the diet, so that what was previously wasted in the faeces and not absorbed was now absorbed and went to build the bones. With regard to respiratory metabolism, he emphasized the importance of sky-shine. The sky was the most valuable source of ultra-violet rays. Bright clouds and blue sky gave even more ultra-violet radiation than the high sun, and far more than the low sun. Respiratory metabolism might also be put up by 100 per cent. in winter, not to any measurable extent by ultra-violet rays, but by exposure to wind and cold air. That was one of the great secrets of open-air treatment; exposure to cold put up the appetite, toned the muscles, and so on, and to this might be added the energetic action of ultra-violet rays and of visible rays also on the skin. In conclusion he (Professor Hill) referred to the need for studying the stimulating and lethal effects of ultra-violet radiation in different doses on the living cell.

Dr. M. WEINBREN said that, in the consideration of this subject, there appeared to be, as in everything else, two kinds of extremists. There were those who put their faith in the value of the short waves, and there were others who believed more in the value of the long waves.

Dr. Leonard Hill had just stated that the sun and clear sky could do everything that artificial sources could do. Luckiesh had shown that the shortest ultra-violet rays to be detected from natural sources were in the region of 2,800 A.U. by the photo-electric cell. In spite of what Dr. Leonard Hill had written and said for a number of years, there were claims that the open tungsten arc would give results which could not be obtained with other sources, because the spectrum from the tungsten arc showed wave-lengths as low as 2,000 A.U. It was known, however, that wave-lengths below 2,400 A.U. could not even penetrate the most superficial layers of the epidermis, and Dr. Leonard Hill had dealt very effectively with this type of extremist. There were, however, the people at the other extreme, headed by Carl Sonne, who pinned their faith to the long visible rays which penetrated to the blood-stream, considerably raising its temperature. Carl Sonne had stated that, exposing a patient for two hours to the carbon arc was equivalent to a pyrexia of about 4° F. for three days, and good results had certainly been obtained with long exposures from the carbon arc. The different sources of ultra-violet rays, however, could not be compared by merely showing their spectra as the spectra did not indicate the amount of energy put out at the different wave-lengths.

Although the proportion of ultra-violet to visible rays might be greater in one source than another, that did not show the relation of the total output of ultra-violet rays between the two sources. Even in the range of the short bactericidal rays, the long flame arc, using the tungsten-cored carbon, would kill off staphylococci or *Bacillus coli communis* in forty seconds at 4 ft. from the lamp. It would take a far longer time with the mercury vapour lamp to get the same effect at this distance. This made the question of dosage a matter of considerable difficulty. No dosage system corresponding to the X-ray system existed. No one could say whether the dose of ultra-violet to be given when treating anaemia should be the same or not as when treating surgical tuberculosis. Moreover, there was no indication as to what percentage of the dose given was effective with succeeding doses. The methylene blue or other gauge might show the same amount of energy being delivered, but that did not mean that the same amount was being absorbed, as the altered condition of the skin would also alter this factor.

Dr. Halls Dally had mentioned high blood-pressure as one of the conditions treated by ultra-violet rays. The results in this condition were by no means constant. The fall in blood-pressure might be very marked in some cases, but other cases failed to respond. Here again one did not know what was the most suitable dose. In one case which he had treated

with the mercury vapour lamp, as there was no response with doses of five minutes and ten minutes; he had ultimately gone on to two hours, and had failed with that too. Another condition mentioned by Dr. Halls Dally as suitable for treatment was early pulmonary tuberculosis. There was some controversy as to whether pulmonary tuberculosis should be treated or not. Of the first fifty cases of surgical tuberculosis which had been treated at Orpington and Sidcup, twenty-two had a demonstrable pulmonary lesion, and some of the others were suspect cases. A number of these suspect cases would no doubt ultimately turn out to be positive. Some of the twenty-two positive cases had chronic and extensive bilateral pulmonary lesions, but even these patients had improved on the treatment.

Bainbridge, dealing with this aspect of tuberculosis in the *Military Surgeon*, in August, 1924, laid great stress on the number of surgical tuberculosis patients who also had a demonstrable pulmonary lesion, and he maintained that even in the cases where no pulmonary lesion could be demonstrated, the pulmonary infection nevertheless existed. It seemed, therefore, that if pulmonary tuberculosis were to be regarded as a contra-indication, a considerable number of surgical tuberculosis patients, who admittedly did well, would have to be denied ultra-violet treatment.

Dr. Weinbren then showed the radiograms of two cases of surgical tuberculosis with pulmonary lesions, in which the patients had considerably improved on ultra-violet treatment.

Dr. ALBERT EIDINOW said that from observations which had been carried out at the laboratories of the National Institute for Medical Research, it had been shown that an "erythema dose" of ultra-violet light applied to the skin of animals increased the hæmobactericidal power of the blood. The same results had been obtained from the effect of radiation on the human skin. In all these investigations it was found that the erythema reaction of the skin appeared to be necessary to give this result. In all the experiments on light it had been shown that ultra-violet rays shorter than 3,000 A.U. were necessary to produce any of the biological reactions which followed light action. These rays were the erythema producing rays. Further investigations which had been carried out had shown that the surface area of the skin irradiated bore a very important relation to the bactericidal response of the blood to light. Small areas of skin, 1 to 5 sq. cm. per kilo weight of rabbits, did not show any improvement in the bactericidal properties of the blood after five minutes or even sixty minutes' exposure. The optimum area of skin appeared to be 20 to 40 sq. cm. per kilo weight of the animals, and the exposure of such skin areas gave a good bactericidal response after five minutes' exposure to the mercury vapour lamp. Ultra-violet irradiation of large areas of skin 80 to 120 per kilo weight failed to improve the hæmobactericidal power with small or large exposures to ultra-violet light. Often a decrease in the bactericidal power was seen.

Although the significance of the hæmobactericidal test was still somewhat in the experimental stage from the clinical point of view, there was little doubt that exposure of the skin to ultra-violet increased the bactericidal power of the shed blood when tested *in vitro*, and that this phenomenon depended upon the production of erythema and the irradiation of a suitable surface area of skin.

From the clinical point of view it had been found that the exposure of the skin of the back up to the iliac crest, roughly an area of 144 sq. cm., usually increased the bactericidal power of the blood of patients who were attending clinics for treatment.

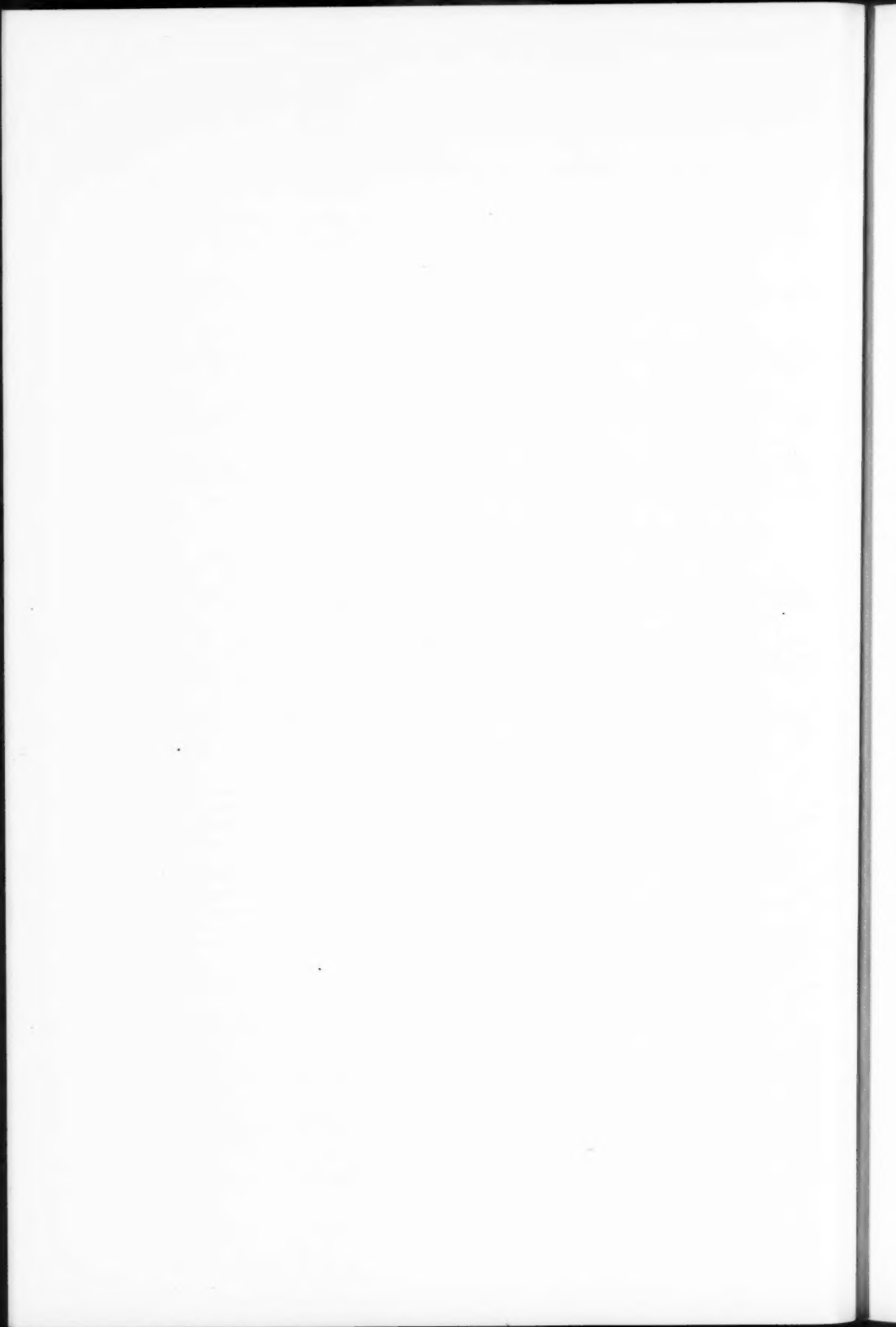
From these observations a technique of treatment had been developed by which dosage was controlled by the surface area of the skin irradiated, and the erythema dose. These light treatments were given each week on alternate days. At each treatment either the front of the chest, the back of the chest, or the front or back of the legs, was exposed. A minimal erythema dose was applied to each area, and a period of 10 to 14 days was allowed to elapse before the area of skin was again irradiated. In this way the skin was allowed to recover to its normal state, and was kept in a light-sensitive condition for even 2 to 3 months, so that a small dose of five minutes' exposure was sufficient to produce an erythema. The skin rapidly became immune and tolerant to ultra-violet rays, even directly after radiation. The desquamating skin was a very effective screen to almost the whole of the ultra-violet rays, and the young skin remaining after desquamation of the horny cells was very sensitive to ultra-violet rays. For these reasons the skin in the desquamating state was never irradiated, and time was allowed to elapse until the skin looked quite smooth and normal before further irradiation was allowed. By these means it was possible to adopt a definite technique of treatment, which it was thought would give equally satisfactory clinical results under the older

methods of treatment in which it was considered that patients had been very much "over-dosed" with light.

Dr. JUSTINA WILSON said that her experience had been chiefly in the treatment of surgical tuberculosis and lupus, skin diseases, rickets, Graves' disease, and certain nose and throat conditions; she emphasized the value of a double method of treatment in most of these, namely, a general tonic ultra-violet radiation, that was to say, a general light bath from four large mercury vapour lamps of the Jesionek type placed in the four corners of the light room. In the light from these, patients walked in moving air from electric fans. This arrangement effected a great saving of time and of *personnel* in supervision of the treatments, while the bodily movement had a bracing effect on muscle tone. Patients obviously ill or with raised temperature, of course, underwent lying-down treatment. All lupus and surgical tuberculosis cases, and nose, ear and throat cases, had, in addition, a more intensive local treatment. This combined irradiation was found to be an important adjuvant in increasing the body's resistance to infection. Except in the more intense local treatments she (Dr. J. Wilson) had not found it necessary to aim at obtaining an erythema dose. The results obtained by a very gradual pigmentation as regards the blood-picture in anæmias, and the reduction of temperature and decrease in size of glands in tuberculosis and in lowered basal metabolic rate in Graves' disease with marked toxæmia, were all that could be wished. But she was interested in Dr. Eidinow's remarks, and was prepared to try this method of giving an erythema dose to one part of the body in a few selected cases, but not in lupus or other forms of tuberculosis.

Dr. ELIZABETH SLOAN CHESSEY said that she was interested in what Dr. Halls Dally had said about the analgesic effect of ultra-violet rays. About a week ago she had examined a patient who complained of intense and almost incessant pain in the pelvis, chiefly in the suprapubic area. The patient said that a "tumour" of the rectum had been removed six months previously. The uterus was normal. A barium enema showed that the rectum was normal, and a later report from the surgeon stated that the tumour was a polypus. An X-ray examination of the bladder, uterus, and kidneys proved negative. The patient mentioned that the pain was sometimes felt down the legs; on further examination there was found to be slight tenderness on pressure over the sciatic nerve between the ischial tuberosity and the great trochanter, and intense pain on pressure over the nerve in the popliteal space. One application of focal rays along the course of the sciatic nerve for three minutes from a tungsten arc lamp markedly relieved the pain and after three applications the pain had practically disappeared.

Dr. HALLS DALLY (in reply) said that he would once again emphasize the importance of the effects of ultra-violet energy in inducing analgesia and in balancing various kinds of metabolism. He was interested in the opinions that had been expressed with reference to the effects in cases of high arterial pressure. He was unable, however, to agree with Professor Leonard Hill's statement that two long flame arcs in series were far more powerful in causing effective ultra-violet radiation than the quadruple arc, for comparison of the spectra of each type photographed under identical conditions (as already thrown upon the screen) clearly showed that the quadruple arc possessed a more even and continuous intensity of ultra-violet radiation than did the long flame arc.



Section of Comparative Medicine.

President—Mr. FREDERICK T. G. HOBDAY, C.M.G., F.R.C.V.S.

Some Diseases of Meat and Their Relation to Public Health.

By GEORGE H. WOOLDRIDGE, F.R.C.V.S., M.R.I.A.

THE subject of this short paper involves the question of meat inspection, the importance of which in relation to public health cannot be over-estimated. By meat inspection is meant the examination of animals in order to determine the fitness of their flesh for human food. Such examination is mainly post-mortem, but meat inspection properly conducted also involves ante-mortem inspection where possible. Meat inspection is mainly concerned with the wholesomeness or unwholesomeness of the flesh of animals, but a subsidiary purpose of it is to prevent what has been called the falsification of flesh, such as the substitution of horse-flesh for beef, &c. Inspection is also necessary in order to ensure (a) the maintenance of sound meat in a wholesome condition and the avoidance of its infection from unsound meat; (b) the detection of unsound meat; (c) the provision of humane and hygienic accommodation for living animals about to be slaughtered.

The conditions which render the flesh unwholesome or unfit for food of man may be ranged under the following heads:—

(1) *Diseased conditions caused by bacteria* which are pathogenic to the human subject, such as anthrax, tuberculosis and actinomycosis, &c.

(2) *Diseased conditions caused by animal parasites* resident in the edible parts and that are pathogenic to man, such as *Trichinella spiralis* and *Cysticercus cellulosæ*, &c.

(3) *The presence of poisonous substances in the flesh*.—Such poisons may come under the heading of (a) bacterial poisons, or toxins generated in the living body by pathogenic bacteria, or produced post-mortem by putrefactive bacteria; (b) mineral or vegetable poisons introduced into the living animal or, in some cases, added to the flesh as a preservative after death.

(4) *Structural alterations that render the flesh or organs unsightly or repulsive in appearance*.—These include extensive neoplasms, tumours, mechanical injuries such as fractures and extensive bruising and lesions caused by parasites that are not pathogenic to man, or that would not infect him if taken in by the mouth. On the latter count one would be justified in condemning the liver of any animal with numerous flukes in it.

(5) *Conditions that render the flesh innutritious, such as emaciated flesh*.—The flesh of new-born animals is somewhat questionably condemned on this ground also. It would seem to me that a better ground in such a case for condemnation would be the repulsive idea and also the fact that such flesh could hardly be regarded as of the nature and substance demanded by the consumer.

There are two ways in which it may be attempted to avert the dangers of unrestricted traffic in meat. First, by instituting what might be described as a fragmentary or incomplete inspection of meat offered for sale, coupled with the infliction of penalties when the sale, or offer for sale, of unwholesome meat or meat otherwise unfit for human food is detected. This method places the duty of determining the fitness of flesh for human food on the butcher, since he has to decide in the first instance whether or not the particular flesh is saleable. Secondly, by instituting a system of general compulsory meat inspection and by making it illegal to sell or offer for sale meat that has not been examined and certified wholesome. This method places the duty of determining the fitness or unfitness of flesh for food on the public authorities. Needless to say, this is the proper and more reasonable way, but it would entail the establishment and compulsory use of public abattoirs.

The former of these methods is in operation in this country, though an attempt has been made to ensure an improved system of inspection by the Public Health (Meat) Regulations, 1924, which provides for three hours' notice being given to the Public Health Officer of the local authority of the intention to slaughter animals for food, unless regular days and times have been previously fixed; or, in the case of emergency slaughter, where notice of the slaughter must be given to the local authority as soon as reasonably possible, whether before or after

the slaughter takes place. These regulations also provide that where, on the slaughter of an animal for sale for human consumption, it appears that any part of the carcase or internal organs is, or may be, diseased or unsound, the person by whom, or on whose behalf, the animal was slaughtered, shall give notice of the fact to the local authority. As I have already intimated, however, these regulations place the responsibility of deciding whether the carcase appears sound or not on the butcher, and it would certainly appear a much more satisfactory arrangement if all carcasses were inspected irrespective of whether the butcher regarded them as being all correct or not.

The objections raised to the institution of public abattoirs and their compulsory use by butchers are largely those of convenience and vested interests, but it has often occurred to me that most butchers would willingly sacrifice these rights if they were assured of immunity from prosecution for the exposure, or sale, of unsound meat, since all meat would be previously inspected and certified by the authorities and the responsibility thus removed from the butchers' shoulders.

Let us now consider some of the diseases of meat in relation to the public health.

(1) *Tuberculosis*.—This is probably the most important disease met with in the food animals, not only on account of its serious nature but also on account of its extraordinary frequency, both in cattle and swine. It is beside the point here to consider whether the so-called human tubercle bacillus and the bovine tubercle bacillus are different organisms or only different strains of the same organism: it is of far greater importance to realize that the so-called bovine tubercle bacillus may, and does frequently, cause serious disease in the human subject. That being admitted, it is very important that every possible step should be taken to prevent what is obviously a preventable disease. In this country, however, it is very rare for flesh to be consumed in an uncooked condition, although it is often eaten somewhat under-cooked, and consequently the danger of infection by eating tuberculous flesh is not very great. All the same it is not at all desirable that the public should be compelled to consume quantities of even dead tubercle bacilli. Meat containing lesions of tuberculosis is obviously unsound and frequently repulsive. It must also contain various toxins of the bacillus, and on those grounds must be regarded as undesirable, if not directly dangerous. I am, myself, unaware of a single authentic case of tuberculosis in the human subject arising from consumption of infected meat. A danger, however, which must not be overlooked, is the possibility of infection by the contamination of other food or utensils with infective material from meat before it has been cooked. The lesions of tuberculosis are in the main confined to the seat of the invasion, or the primary lesion, and the lymphatic glands associated with the part. It is, therefore, most commonly a local disease, and condemnation of the parts containing the primary lesion and the corresponding glands is usually sufficient to ensure the safety of the public, provided the carcase is well nourished and otherwise sound. When the blood-stream, however, has become infected, either by way of the lymphatics or by the lesion involving a blood-vessel, generalization takes place, and, in the majority of cases this is indicated by a miliary tuberculosis of both lungs. In some instances the arterial blood-stream becomes involved and generalization is then shown by lesions in deeper-seated lymphatic glands, in or between the muscles, and in other tissues such as bone. It is obvious that in such cases total seizure must be enforced. A problem, however, presents itself in those cases in which, although the lesions from their distribution must be regarded as local tuberculosis, they are yet multiple and extensive. Careful discretion must be exercised in such instances as to whether or not the condition must be regarded in the same light as though it were generalized in the strict sense, or whether some extensive local seizure will safeguard the public. I am constrained to put this point forward because, although the public health is the main issue, it must never be forgotten that a butcher's right to his own property is also very important and one has no justification in confiscating his property unless one is fairly sure that it is a potential source of danger, or is otherwise unfit for human food. The matter might be looked at in a different light if there was any system of compensation for the seizure of the flesh of animals killed in good faith. In such cases the seizure is for the public health and it would be only reasonable to suggest that the public should pay for it. It must be admitted that any general system of compensation might readily be abused by fraudulent butchers and others, but this could be well checked where public abattoirs were in use and where all animals were inspected preceding slaughter by the veterinary inspector.

Some differences of opinion have arisen with regard to the importance of tuberculosis in swine, largely owing to the recommendation of the Royal Commission on Tuberculosis of 1898, in which it was recommended that in the case of any degree of tuberculosis of swine

total seizure should be practised. This recommendation was probably made in view of the great tendency to generalization in the pig. Of course one knows that it is impossible to tell at what time generalization may have occurred, and the carcass may have become recently invaded and slaughtered before there was time for the development of lesions. Practical experience, however, has shown that in very many cases there is a purely localized tuberculosis in swine, and most experienced inspectors realize the injustice of total seizure; they therefore deal with such cases on their merits as localized cases, in the same way as with regard to carcasses of beef. This method is my interpretation of what has been recommended by the Ministry of Health in Memo 62, "Foods." Any degree of tuberculosis in swine, however, should necessitate a very thorough general examination, including in every case the splitting of the carcass through the spinal column, since so many instances arise in which the vertebræ are involved in well-nourished carcasses which would otherwise have been passed for food.

In estimating the importance of localized tuberculosis in either species, particular attention should be paid to any sequence of lymphatic glands affected, since some groups may be regarded as a second line of defence, and, if they are involved, it implies that the primary infection and the corresponding glands have been overcome. In such a case the disease is obviously more advanced and more serious. From this point of view the greatest importance must be attached to the pre-pectoral lymphatic glands in regard to the forequarters and the iliac and the deep inguinal glands with respect to the hindquarters.

(2) *Actinomycosis*.—This disease is met with in cattle and swine and to a less extent in the human subject. It is doubtful, however, whether there is any authentic case of a human being becoming infected by the consumption of the flesh of animals affected by actinomycosis. There is, however, a danger of infection by inoculation through handling of the flesh before cooking. Generally speaking, in both cattle and swine there are no systemic effects unless the lesion has interfered with mastication or deglutition. It is almost always a purely local disease and in a well-nourished carcass perfect safety is ensured by practising local seizure of the affected parts, such as the head and the glands of the throat, or the mammary gland and its lymphatic glands. In only very rare cases does generalization take place, lesions then occurring in the internal organs, such as the liver and lungs.

(3) *Anthrax*.—There are two ways in which anthrax carcasses find their way into the slaughter house. The first and most frequent way is through the slaughter of an animal at the point of death, the nature of the disease being unknown, though possibly sometimes suspected; and second, the slaughter of an animal supposed to be healthy during the incubating stage of the disease. The flesh of anthrax carcasses which have been allowed to die with the blood in them, or have been slaughtered too late to permit of efficient bleeding, is unusually dark and could not fail to attract attention. It is stated, however, that when animals suffering from anthrax are killed sufficiently early to enable them to be well bled the muscular tissue is of abnormal pallor. Such carcasses might easily escape detection. There are numerous cases of anthrax carcasses having been retailed and consumed without reported ill-effects, some of which have only come to light through the development of a lesion by the butcher, or other person, handling the meat as the result of inoculation. There can be no doubt that all anthrax carcasses should be condemned, though the danger of causing anthrax is enormously reduced, if not entirely removed, by cooking. This, however, does not remove the danger due to handling infected material.

(4) *Foot-and-Mouth Disease*.—This disease is communicable to the human subject, but again I am unaware of any authentic instance of its being communicated through eating flesh. The probable danger is of inoculation through handling parts containing the lesions. In this country it is more than likely that the danger of its spread in animals would be considered a stronger justification for condemning the carcass, but on the continent it is the main practice to confiscate the parts with lesions and to pass the other portions if properly bled and well set.

(5) *Rabies*.—The flesh of animals slaughtered while rabid must be condemned, because of the danger of handling. There is no known instance of the disease being contracted by eating the flesh. There can be no objection whatever to passing the carcass of animals that have exhibited no rabid symptoms but have been slaughtered because they have been bitten by a rabid dog. All that would be necessary would be to remove the parts that had been damaged by the bite.

(6) *Bacterial diseases caused by organisms not pathogenic to man, such as swine fever, swine erysipelas, pleuro-pneumonia, blackleg, &c.*—The course to pursue in the case of these infections must depend entirely on the condition of the animal at the time of slaughter and on

the condition of the carcase as revealed afterwards. In each case if the animal was in an acute phase of the disease the carcase would undoubtedly show the condition generally recognized as fevered flesh and in this case would undoubtedly justify condemnation. If, however, the animal has been slaughtered in a quite early stage of the disease and there is no evidence of injurious effects on the body in general, the carcase may be passed. It must, however, be well nourished, the carcase thoroughly bled and the flesh firm and otherwise normal in appearance. The diseased parts must never be passed, and, in the case of blackleg it is doubtful whether any part of the carcase would be marketable. I have personal knowledge, however, of numerous instances in which the affected quarter of a calf suffering from blackleg has been destroyed and the remainder eaten with impunity.

(7) *Carcases of animals that have been poisoned.*—It is a not uncommon belief that the flesh of animals that have succumbed to any powerful poison, vegetable or mineral, is dangerous as the food of man, but experiments have negated this view. It has been shown that in the case of animals poisoned even with the most powerful alkaloids administered by the mouth, such as strychnine, a pound of the muscular tissue would not contain a sufficient quantity of the poison that would be harmful to man by ingestion. The risk is even less in the case of strong mineral poisons. There is, therefore, no occasion to condemn the carcase of poisoned animals provided they have been killed before such constitutional effects as degeneration of the heart-muscle or liver have set in, and in time to allow them to be perfectly bled and to allow the carcase to set firmly. This applies also to the case of animals that have received quantities of medicinal substances, provided always that these have not tainted the flesh and that the condition for which the medicines were given does not of itself justify the condemnation.

(8) *Fevered Flesh.*—The meat which inspectors designate as "febrile" is that which has undergone certain changes characterized by alteration of the colour of the muscles, infiltration of inter-fascicular connective tissue with oedema and the production of a peculiar odour. It is not necessary that the animal in question should have been affected with a high temperature, for similar changes may be brought about in the absence of pyrexia. Fevered flesh may be recognized by the following characters. When first cut the muscle is of a reddish brown colour, rather darker than normal, but turns pink, or brighter, on exposure to air. The oedema makes the meat soft, flabby and sticky to the touch, and when cut there may be a slow exudation of clear pink serum making the surface moist; the capillaries are engorged, indicating imperfect bleeding, as is best seen under the shoulder and in the flank. The fat is sometimes firm, at other times soft; sometimes pink, at other times white. The serous membranes have frequently a leaden tinge. The odour is peculiar and characteristic but passes away on exposure. It is best observed when the shoulder is separated from the forequarter. The vertebræ have an unnatural brown colour when sawn through, but become brighter on exposure. The flabbiness of the carcase is shown by the muscles bulging over the symphysis pubis when hung up by the hock. The forequarter is also easily moved on the trunk owing to the soft state of the muscles. Microscopically, there is cloudy swelling of the muscle-fibres which are swollen. The striæ have disappeared and nuclei stain badly. There may be infiltration with leucocytes. Organisms of some kind are always to be found and they may include bacilli of the colon type, paratyphoid and Gaertner bacilli, streptococci, and staphylococci. Specific organisms may also be found in the pulp of lymph glands, such as *Bacillus anthracis*, &c. No matter what is the origin, febrile meat contains toxic properties, such as alexins and other complex proteid materials. It is, therefore, unfit for consumption, even after sterilization. Organisms may be killed but the toxins may remain. In my view it is usually meat of this kind that is responsible for most of the cases of meat poisoning in man.

Another potent source of meat poisoning is the flesh of animals killed in emergency and where the blood-stream has been invaded by various organisms from the alimentary tract immediately before slaughter. The danger in such a case is all the greater because every part of the carcase is involved, and there may be no gross change to attract attention. Carcases of this character may easily pass in any system of fragmentary inspection such as is here practised, but that would be quite impossible if compulsory abattoirs were established, entailing, as I maintain should be the case, ante-mortem inspection.

Decomposition or taint due to sound meat having been kept rather long and to the invasion of putrefactive organisms from outside sources is of very small importance in comparison with the former, although it may be more easily observed by the sense of smell. An

interesting point, especially in a legal sense, may be involved as to the wholesomeness or unwholesomeness of such flesh apart from any æsthetic judgment. Many so-called epicures prefer their meat "high" and consider it hardly fit to eat unless it is "high" (or in the opinion of others "over-ripe"), and they certainly are not adversely affected by eating it. The same flesh might readily cause nausea and alimentary disturbance in other people. But the same thing may be said of perfectly fresh and sound pork, and no butcher could reasonably be prosecuted for selling such pork because it made some people ill.

I am afraid I have only been able to touch the fringe of this great subject and I must plead for indulgence owing to the recent general unrest, caused by the Strike, and my inability to devote the time to the matter that I had hoped to do. However, I trust there may be sufficient material and that I may have made sufficient unorthodox statements to stimulate an interesting and instructive discussion.

Discussion.—Lieutenant-Colonel T. DUNLOP-YOUNG: Professor Wooldridge advocates ante-mortem inspection. I have long urged this necessary part of meat inspection, for no system is complete without it and in all the countries I have visited viewing meat inspection, the ante-mortem examination is considered of great importance not only in the detection of "suspected" animals but in the control of contagious disease. Practically all imported meat in Smithfield bears a stamp or label showing that ante-mortem and post-mortem examination has been made by a veterinary officer.

In speaking of actinomycosis, the lecturer mentioned the danger of handling this disease. I am not aware of any reported cases of inoculation caused by handling actinomycotic lesions.

The statement that the butcher is held responsible as to whether a carcass is or is not diseased has to a great extent been modified by the Meat Regulations, as the duty of the butcher now is to report any abnormal conditions he observes, and he has the important protection that if he asks that the carcass, after examination has been conducted, be stamped by the inspector and it is stamped, neither he, nor any other butcher to whom he sells the stamped meat, can be prosecuted if any inherent disease is subsequently found in the carcass. I am surprised that butchers do not make more use of this protection.

Professor Wooldridge used the word "generalization" when speaking of the blood-stream becoming invaded by the tubercle bacilli. I do not think he can have meant that, as it is evident from isolated lesions found in bone, &c., that although the bacilli gain entrance to the blood circulation the few bacilli which enter generally become located in one, or perhaps two areas, and generalization rarely takes place. In fact, in meat inspection, although many carcasses and their organs are extensively infected, very few are what could be strictly termed "generalized" tuberculosis; this opinion, I believe I am right in saying, is held by no less an authority than Sir John MacFadyen. With regard to the disease in pigs I think I can say without egotism that the method of dealing with pig carcasses described by the lecturer as recommended by the Departmental Committee on Meat Inspection was first brought into daily use at Smithfield and has been the means, without injury to the health of the public, of saving thousands of pounds yearly. I should like to call attention to an important feature which has come under our notice lately—that is, in slaughterhouse inspection—namely, that if lesions of tuberculosis are found in the lungs and their glands only, or in combination with the mesenteric glands, no other lesions being apparent in the carcass, that carcass is passed for sale. In several of such cases where slight evidence of the disease still remained *in situ* in the posterior mediastinal lymph-glands, the vertebræ have been split and lesions found therein. In one case thirteen centres were found in the vertebræ. It would therefore appear that whenever lesions of tuberculosis are found in a pig carcass or its organs, the vertebræ should be split before passing the carcass for sale. The lecturer said anthrax carcasses had been eaten and did not injure those who consumed the meat. That is so—there are several cases on record; the gastric secretions evidently destroy the bacilli *if no spores are present*; but there is great danger of handling such carcasses. Here, again, ante-mortem examination is useful. In more than one case we have found that the affected animal arrived at the lairs exhausted, breathing rapidly, lay down immediately it arrived and showed a frothy red-coloured discharge from the nose and mouth. Professor Wooldridge, in his remarks on foot-and-mouth disease, said it was not necessary, except to prevent spread of the disease, to condemn the carcasses and that "contacts" could be used for human food. That appears to be true, but we must not forget that the blood of animals in the incubative stage, that is, before vesicles are formed, is very infective and may be the means of spreading the disease. He also mentioned the custom of destroying the affected quarter in blackleg disease and consuming the other three quarters.

Not uncommonly, parts of such carcasses are sent to Smithfield; in fact, when we get only three quarters of a calf carcass sent, we are at once suspicious and the bacilli are easily found in the tissues. The type of carcasses which cause most trouble to inspectors in markets, and some of which are most dangerous from a meat poisoning point of view, are "emergency cases," including polyarthritis septica, septic metritis, septic mammitis, swine erysipelas, malignant œdema, &c.; mention may also be made of a disease which is causing us some concern, namely, caseous lymphadenitis. Such carcasses, minus the organs, require examination by officers who have had an extensive pathological and bacteriological training with a constant use of the microscope. The Meat Regulations constitute an attempt to set up some system of meat inspection in England, where so far, with the exception of large towns, there has been, strictly speaking, no meat inspection. Those regulations are useful as a beginning, but are insufficient, and in the majority of places the work is entrusted to men who have only had a few weeks' training. I cast no reflection upon them; doubtless they do their very best, but it must be obvious that they cannot be good at all branches of their sanitary work. I do not include lay inspectors specially trained, who do no other work than meat inspection. Nevertheless, the Royal Sanitary Institute and gentlemen like Dr. Porter, who takes a great interest in the subject, are to be congratulated on what has been done to give those men some idea of what should or should not be passed as fit for human food. It may seem incredible, but the inspection of meat accepted for the Army and Navy is conducted by officers who have no scientific training and only a few weeks' practical and theoretical training. Again, I am not in any way suggesting that those officers do not act up to the best of their abilities; it is the system I refer to, not the officers. This is the work that should surely be done in the Navy by medical officers, and in the Army the meat inspection could be done by officers of the R.A.V.C., while "other foods" could be inspected by officers of the R.A.M.C. at no extra expense to the country.

It will be difficult, if not impossible, to do away with all private slaughterhouses; 90 per cent. of the butchers using them kill very good-class animals. Here and there places exist where the tenant will kill anything he can buy; there are rogues in all trades and professions: those can be singled out and dealt with. In all large towns public abattoirs should be erected and private slaughterhouses closed, as in Scotland. In county districts a Chief Veterinary Officer should be appointed just as a Chief Medical Officer is appointed; he could supervise meat inspection, the examination of animals under the Tuberculosis Order and Contagious Diseases Orders. In districts, local veterinary surgeons could, as in Holland, supervise meat inspection as part-time officers; the lay inspector could pass all healthy carcasses or those in which the organs only are slightly affected with unimportant lesions; but where the carcasses are affected, they should be detained until seen by the local veterinary surgeon. All cases of dispute, or instances where bacteriological examination is necessary, should be referred to the Chief Veterinary Officer, who could, if necessary, confer with the Chief Medical Officer.

Until some such organization is adopted, we shall continue to suffer from a system of imperfection. It is for the medical profession, in the interests of public health, to urge that this should be done, and in so doing they will have the united support of the veterinary profession in an endeavour to obtain the elimination from our text-books on pathology the words "in England there is no regulated system of meat inspection."

Dr. GEORGE JONES: Much has been said about criminal responsibility of sellers of meat: so far the civil liability of the seller to the buyer has not been mentioned. If one goes into a restaurant and orders a meal there is a contract inferred from conduct between the visitor and the restaurateur. If, in consequence of the joint being bad he is ill, he has an action at law against the restaurateur, and may obtain heavy damages from him. The restaurateur may have a remedy over against the butcher who sold him the meat, and the butcher may have a remedy over against the wholesale dealer at the market, and he, in turn, against the slaughterer, or the grazier, or the farmer. Now the slaughterhouse owner may be induced to sell his rights in his premises to the municipality all the more readily because he is almost certain to be asked to run his own or new and better premises on behalf of the municipality. Should statutory powers be obtained for the reconstruction or redistribution of existing slaughterhouses a complete scheme for examination and marking of meat might be adopted. A clause in the Act might well give statutory protection to the seller of meat marked as examined and found good by the municipality, and it might be enacted that such a warranty—for such it would be—should bar any subsequent action, unless gross negligence was proved as against some servant or agent of the municipality.

The private lunatic asylum, the private elementary school, even the great voluntary hospitals are being hard pressed by the still greater municipal asylums, by the council schools, and by the Poor Law "Hospitals." Is not this an indication that before long municipal abattoirs will displace the existing slaughterhouses?

The economic aspect may prove important. It can hardly be advantageous to drive cattle through Stratford, Bow, Mile End and Whitechapel, to the old slaughterhouses in Butcher's Row, Aldgate. In the middle of the eighteenth century the London Hospital bought four farms which ran back from the present site in Whitechapel Road to the river. In those days the Aldgate slaughterhouses were no doubt commodious and convenient. Now they are not, and the local Medical Officer of Health, the traffic authorities and the travelling public will be very glad to hear that Butcher's Row is to migrate to Islington.

There is yet another economic advantage in the concentration of the meat trade and the re-organization of slaughtering. The production of commercial albumen from blood, the extraction of the internal secretions of the ductless glands, the disposal of hides and offal, could all be carried on with far greater economy if scattered slaughterhouses disappeared and the trade were concentrated in a few well-selected areas.

We have seen in the lifetime of a generation one great industry after another organized, centralized, and at last municipalized, until in such towns as Glasgow and Birmingham nearly everything is in the hands of the Corporation. May not the advocates of municipal abattoirs hope for something similar in the not far distant future?

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SECTION OF DERMATOLOGY WITH THE SECTION
FOR THE STUDY OF DISEASE IN CHILDREN.

(JOINT DISCUSSION No. 5.)

December 17, 1925.

DISCUSSION ON THE ÆTIOLOGY AND TREATMENT OF
INFANTILE ECZEMA.

Dr. A. M. H. GRAY (pp. 71, 83), Dr. H. C. CAMERON (pp. 74, 83), Dr. H. G. ADAMSON (p. 77), Dr. F. LANGMEAD (p. 78), Dr. J. M. H. MACLEOD (p. 79), Dr. G. H. LANCASHIRE (Manchester) (p. 80), Dr. HALDIN DAVIS (p. 80), Dr. MURRAY BLIGH (Liverpool) (p. 81), Mr. FRANK COKE (p. 82), Dr. S. E. DORE (p. 82), Dr. M. SYDNEY THOMSON (p. 82), Dr. J. H. SEQUIERA (Chairman) (p. 83).

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Section for the Study of Disease in Children.

President—Dr. H. C. CAMERON.

Meeting held at the National Hospital for the Paralyzed and Epileptic, Queen Square, W.C., March 27, 1925. Chairman—Dr. F. J. POYNTON.

A Family with Progressive Familial Cerebral (so-called Cerebro-Macular) Degeneration.

By W. J. ADIE, M.B.

Family History.—Parents alive and well, no history of mental or nervous disease in other branches of the family. Children: (1) Boy, aged 14 years (shown); (2) Girl, died, aged 10 years (accident); (3) Boy, died aged 3 months (tuberculous peritonitis); (4) Boy, aged 8 years (shown); (5) Boy, aged 5 years (shown); (6) Premature (stillborn); (7) Boy, aged 1½ years (shown).

The onset of symptoms occurs in this family during the seventh year of life with slow mental deterioration, convulsions, visual failure with optic atrophy and retinal degeneration, progressive spastic weakness of the muscles and curious, involuntary jactitations. When first I saw the two oldest children the disease was well established. The second boy shown was then aged 6 years, and was still normal except for early retinal changes. The two youngest are still perfectly healthy children with normal fundi.

The disease called familial cerebro-macular degeneration presents itself to us in several more or less distinct forms; the one with which we are most familiar is the amaurotic family idiocy associated with the names of Tay, Sachs and Schaffer. This, the *infantile type*, begins in the early months of life and is characterized by progressive loss of muscular power, progressive visual failure with the typical cherry-red spot at the macula, rapid dementia, and death within a year or so.

In the form exhibited by the family to which these four patients belong—the *juvenile type*, associated with the names of Spielmeier, Vogt, Batten and others—the onset is at about the time of the second dentition. In this family, the earliest symptoms noticed by the parents are "twitchings and tremblings" which begin soon after the age of 6 years. In this form the triad—paralysis, loss of vision and dementia—is fairly constant; the course is slower than in the infantile form—this boy J. is in his fifteenth year—there is no cherry-red spot at the macula, but there is a kind of retinitis pigmentosa beginning in the macular region, or optic atrophy, or, as in this family, both, and in contrast to the infantile form, the clinical features show considerable variations in different families.

The third form—the *late infantile type* of Jansky and Bielschowsky—appears about the age of 8 years and ends in death in about three or four years. In this type there is no cherry-red spot but there is usually optic atrophy without retinal changes.

It will be understood that these types are merely different forms of the same disease; formerly certain pathological findings were supposed to be peculiar to each form, but this has been disproved. It is important to remember that in some families, or in some members of an affected family, one of the cardinal signs may be absent. For example, there may be no retinal change, no optic atrophy, no failure of vision. Further, an undoubted case has been described in which only one member of a family was affected.

The only constant feature of this disease is the peculiar histological change first described by Schaffer in the ganglion cells and their dendrites. The ganglion cells are of an enormous size, and a peculiar lipid pigment is seen within them. It used to be thought that this change was universal throughout the nervous system, but this is not so; any part of the brain may be spared, hence the different symptomatology in different cases, and the absence of blindness in some. A photograph of the brain of a patient who died from this disease shows the small size of the cerebellum, a feature that has been noted in several cases. In one case the clinical diagnosis of congenital atrophy of the cerebellum seemed to be confirmed by the naked-eye appearance of the brain, but microscopic examination showed changes typical of amaurotic idiocy in several parts of the brain and cord.

Discussion.—Dr. F. PARKES WEBER said that Dr. Adie, in his summing up of the various diseases of development in which changes in the retina and optic nerves occurred, had not included the syndrome of adiposo-genital dystrophy associated with some form of pigmentary retinal degeneration (retinitis

2 *Adie: Case of True Narcolepsy; Amytonia Congenita*

pigmentosa). This was now known as Biedl's syndrome and might be accompanied (like other postnatal disorders of development) by antenatal abnormalities of development, such as the presence of six fingers or six toes (cf. the case of the boy shown by Dr. Douglas McAlpine at the Section of Neurology on March 12, 1925). Biedl's syndrome might be familial, as in some of the cases described by A. Biedl himself, S. Solis Cohen and Edward Weiss of Philadelphia propose to call it the "Laurence-Moon-Biedl syndrome," because of a paper by J. Z. Laurence and R. C. Moon in the *Ophthalmic Review*, London, 1866, ii, pp. 32-41, entitled "Four Cases of Retinitis Pigmentosa occurring in the same Family and Accompanied by General Imperfections of Development." He (Dr. Weber) had recently seen a man, aged 40, with retinitis pigmentosa, obesity and sexual impotence—apparently a minor, isolated (non-familial) example of Biedl's syndrome. Probably non-familial examples would turn out to be commoner than familial examples.

Dr. DONALD PATERSON said that amaurotic family idiocy was a disease largely confined to Jews.

Dr. ADIE (in reply) said he was interested in Dr. Parkes Weber's remarks about the Biedl syndrome. Did Dr. Weber think the condition was allied to cerebro-macular degeneration? To decide this point a post-mortem examination would be necessary; if the typical cell-changes of Schaffer were present then the conditions were allied.

In reply to Dr. Paterson he said that in the infantile type there was a high preponderance in Jewish families; in the late infantile and juvenile types there was no such preponderance, in fact most of the cases had occurred in Gentiles.

A Case of true Narcolepsy: Onset at the Age of 12 Years.

By W. J. ADIE, M.B.

THIS girl came to the Hospital two years ago, when a diagnosis of minor epilepsy was made. The disease from which she suffers, however, has nothing to do with epilepsy; she has attacks in which she simply falls asleep. They are most frequent when she is tired or has nothing interesting to do, but they may occur at any time. It is sometimes possible for her to ward off the attack for a time by moving about actively, but sleep she must, sooner or later, and the longer she resists the inclination the more soundly she sleeps. In the attacks she presents every appearance of being in normal sleep; she can be roused easily and feels no ill-effects afterwards. She exhibits another interesting symptom—if she laughs heartily she has difficulty in standing, and sometimes she has fallen down. In her own words: "If anyone tells me a joke and I see it very much, my eyes go misty, I feel funny in the head, my knees give way and I feel as if I may fall down." You might suppose that this "laughing symptom"—I cannot think of a better name—is fortuitous, but I have seen four other typical cases of narcolepsy in which it was present.

I have seen this girl and her mother frequently during the last year, and have never been able to elicit anything from them that would support a diagnosis of epilepsy. I have called the case one of *true narcolepsy*, because unfortunately the word "narcolepsy" is used in connexion with several other forms of pathological sleep. It should be applied only to cases in which frequent attacks of natural sleep of short duration—from a few minutes up to half an hour—occur in otherwise healthy individuals; the disease is of long duration and entirely uninfluenced by treatment. It is quite distinct from *pyknolepsy*, although the name "short narcoleptic attacks" was applied to it by Friedmann.

Narcolepsy is described in text-books as a disease of adult life; the youngest case hitherto on record is that of a boy aged 18 years. I thought it might interest the members of this Section to see a patient in whom the disease began at the age of 12 years.

Dr. F. J. POYNTON (Chairman) said he had once had a curious case—that of an adult patient who suffered from attacks of this type, and the remarks of Dr. Adie about the effects of laughing were of interest. If anyone bored this patient, he vomited. On one occasion he had his landlord to see him for the week-end—a man of poor conversational ability—and the patient was so much bored by him that he had to leave the dinner table and be sick. He (the speaker) supposed that this was due to the same kind of susceptibility of nervous tissue that linked laughter with faintness.

A Family Affected with Amytonia Congenita.

By W. J. ADIE, M.B.

The S. family.—Parents, seven uncles and thirty-seven first cousins all healthy. Thirteen children: (1) female, healthy; (2) female, healthy; (3) female, stillborn; (4) male, affected, shown; (5) female, affected, shown; (6) female, affected; (7) female, affected, died of measles; (8) female, healthy; (9) male, healthy; (10) female, affected, shown; (11) male, healthy; (12) female, healthy; (13) male, congenital dislocation of hips, otherwise healthy. Mother now pregnant.

These children show very well the characteristic features of the disease; the extreme flaccidity of the limbs and trunk which allows us to place them in grotesque attitudes, the smallness of the muscles, without real atrophy, the diminished power—without real paralysis, the diminution but not loss—of faradic irritability and the absence of knee-jerks characteristic of the early stage. The youngest affected child, F., aged 5 years, is now able to sit up, as you see, but she cannot stand. One of the girls began to walk at the age of 2 years, and is now perfectly well at the age of 13 years. The girl G., aged 14 years, walks very well, but she is still hypotonic and the muscles are small and weak.

I have known the eldest boy, A., since he was 4; at that age he could sit up but could not stand; he is now aged 18 and is employed in a florist's shop. He gets about very well but cannot run like other boys, and has some difficulty in climbing stairs. The tendency to progressive improvement, one of the characteristics of the disease, is well shown in this family.

Case of Post-diphtheritic Hemiplegia.

Shown by REDVERS IRONSIDE, M.B., for C. M. HINDS HOWELL, M.D.

I. S., aged 11 years, five years ago suffered from a severe attack of diphtheria with hæmorrhage from the nasopharynx and bowels, and hæmaturia. The laryngeal condition necessitated tracheotomy. The attack left her with paralysis of accommodation, palatal paralysis and with a right hemiparesis. Since then the ocular and palatal paralyses have disappeared but the hemiparesis remains, accompanied by the writhing athetotic movements of the right arm and leg which you now see. The right upper limb between the spasms is very hypotonic, especially at the elbows and fingers; the right lower limb is shorter by half an inch than the left and shows a little contracture of the tendo Achillis. There is rapid, fine nystagmus on lateral deviation of the eyes, and the left pupil is larger than the right. There is no hemianopsia nor sensory defect; the fundi are normal.

The first case of this kind was described in 1859 by Sir William Gull (a former Governor of this Hospital). It differs from all other varieties of diphtheritic paralysis in that the damage to the nervous system is not primary but is secondary to changes in the blood-vessels, either embolism or thrombosis or hæmorrhagic encephalitis.

Dr. J. D. Rolleston has collated reports of eighteen necropsies in this condition. Many of the cases showed endocarditis with embolic changes in the cerebral blood-vessels. This child has no endocarditis; I think she has had a hæmorrhagic encephalitis. Hemiplegia as a residue of diphtheria is excessively rare.

Dr. J. D. Rolleston said that in his twenty-five years' association with infectious disease hospitals he had seen only about twelve cases of the kind shown by Dr. Ironside. Though the majority of such cases recovered, i.e., though the prognosis *quoad vitam* was good, it was bad in regard to complete recovery; patients were left with some infirmity, mental or physical, perhaps both. Still, there had been remarkable exceptions to that rule. Some years ago¹ he (the speaker) had published notes of two cases of transient hemiplegia in diphtheria in which the patients had recovered completely. Were these cases due to minute emboli, or to cerebral œdema? In most of the cases of permanent hemiplegia the condition was shown at autopsy to be due to emboli.

More rarely than hemiplegia there occurred other forms of embolism in diphtheria, one of the most dramatic being gangrene of the leg. Marfan considered it to be due to an apical endocarditis, which caused cardiac thrombosis, so that emboli were carried into the vessels of the limbs. Sometimes the spleen and kidneys were involved. In the post-mortem examination he had made on one case of diphtheritic hemiplegia he also found splenic and renal infarcts. Hæmorrhagic encephalitis had been discovered in a few cases, but it was very rare. Hemiplegia was more common in diphtheria than in any other infectious disease; it was rare after typhoid and scarlet fever, though he had recorded three examples of post-scarlatinal hemiplegia.² Judging by some neurological text-books one would conclude that it was a common sequel of acute specific fevers, but that was a great mistake, as also was the statement about the frequency of nervous sequelæ after measles.

Case of Cardiac Infantilism.

By MACDONALD CRITCHLEY, M.D. (for J. RISIEN RUSSELL, M.D.).

THE patient, a boy aged 15 years, is an example of infantilism due to congenital heart disease. He is the eighth child, the other members of the family being healthy. The mother states that the pregnancy and confinement were normal; the infant was born at full term and

¹ *Rev. Neur. and Psych.*, 1916, xiv, p. 145.

² *Ibid.*, 1908, vi, p. 430.

weighed 7 lb. He cut his teeth, sat up, talked, and walked at the proper times, but it was noticed that his skin very easily became blue and was over-susceptible to the cold. Whilst at school he was unable to play games, run about or climb stairs.

At present he shows distinct infantilism, his height being only 4 ft. 1 in. (normal 5 ft. 2 in.). His weight is 3 st. 10 lb. (normal 7 st. 5 lb.). There is a slight cyanotic tinge to the lips and ears; fingers and toes show an extreme degree of clubbing. Respirations are noisy and laboured—resembling those of an asthmatic. There is no history of epistaxis or hæmatemesis but the patient suffers from piles. The thorax is barrel-shaped, the sternum being prominent, and there is a distinct Harrison's sulcus. A wavy, apical impulse is visible in the fifth space in the nipple line; a systolic thrill can be palpated at the base of the præcordium. The area of cardiac dullness is increased laterally and slightly upwards. On auscultation a long blowing murmur, loudest at the pulmonary area, persists throughout systole and well into diastole. It is inaudible behind. No accentuation of the second sound.

There is no polycythæmia.

A skiagram of the chest shows distinct enlargement of the right and left ventricles and also of the bulbus cordis.

Mentally the lad is very alert; he left school a year ago, having attained the seventh standard.

[May 22, 1925.]

Case of (?) *Lymphocytic Leukæmia*.

By HUGH THURSFIELD, M.D.

THE patient, W. W., aged 4½ years, was in good health up to January of this year, when the glands in his neck and axillæ began to enlarge. His mouth at this time was inflamed and ulcerated. The tonsils had been removed two years previously.

On admission to hospital, January 23, 1925, he was very anæmic; there were some purpuric spots on his back, and marks like bruises on his legs. The cervical, axillary and submaxillary glands were enlarged, firm, discrete and painless. On the scalp there was a hard, rounded, painless swelling beneath the skin, but not attached to the cranium. The liver was enlarged two and a half finger-breadths and the spleen was just palpable. A blood-count showed red blood-cells, 3,200,000; white blood-cells, 7,800, 96·5 per cent. of which were lymphocytic cells. The number of blood-platelets per cubic millimetre was normal.

During February and March the patient's condition became progressively worse, and a fatal termination was expected. The right side of the face swelled up, and there was some swelling of the mandible on the right side posteriorly. Epistaxis and melæna occurred, fresh purpuric spots appeared on the trunk, fluids were sometimes regurgitated through the nose on drinking and the patient was almost aphonic. Numerous retinal hæmorrhages. The white blood-cells, estimated on two occasions, had fallen almost to 1,000 per cubic millimetre, the majority being lymphocytic cells.

Towards the end of March a gradual improvement commenced. On the 27th the right ear began to discharge profusely. Streptococci were isolated. In April the swelling in the scalp had disappeared and the axillary glands were much smaller, only those in the submaxillary region remaining large; they were never tender. Red cells numbered 3,700,000; white cells, 10,000.

On May 8, 1925, a blood-count showed red cells, 5,040,000; white cells, 10,000; 61 per cent. lymphocytes. The submaxillary glands were still palpable and the right side of the face swollen.

When patient was last seen, May 19, 1925, several hard, painless lumps had appeared in the scalp, but were freely movable over the underlying bone. A small sequestrum of bone had separated from the posterior part of the right half of the mandible.

The patient appears in fairly good health.

(1) Is this a case of lymphocytic leukæmia which has reached a stage of quiescence? (2) If it is not an acute lymphocytic leukæmia, is it conceivably such a case as is reported from time to time in which suppuration, instead of producing polymorphonuclear leucocytosis, produces a lymphocytic reaction? (3) Lastly, what are the lumps on the head, and what is their probable course? The mother says they have twice come and gone.

Dr. F. PARKES WEBER said he also thought the case was a form of leukaemia—or rather, perhaps a leukaemic lymphadenosis, the total white-cell count being not high. The nodules in the scalp were probably lymphoblastic, though some had disappeared. The improvement might be due to the infection and might be only temporary.

Postscript.—This patient died on June 16, and at autopsy the diagnosis of lymphocytic leukaemia was confirmed.

A Case of (?) Renal Sarcoma showing remarkable Improvement after Varicella.

Shown by J. DAVIS, L.R.C.P.Lond., M.R.C.S.Eng.
(for DONALD PATERSON, M.B.)

R. A., AGED 4½ years. The child was admitted with a history of constipation and periodic distension of the abdomen, loss of weight, and for two years occasional vomiting. The abdomen was found to be greatly distended, with two palpable masses, one in the left iliac fossa and the other in the right lumbar iliac region. Under an anæsthetic the masses were found to be hard and nodular, and seemed to be attached to the posterior abdominal wall, and fixed. A diagnosis of renal sarcoma was proposed. Bone—normal. Wassermann reaction and tuberculosis tests—negative. Blood—moderate anæmia. After becoming gradually worse, with progressive distension of the abdomen and loss of weight for about eleven weeks, the child rapidly became much better, gaining 2½ lb. in a week. Ten days later a typical varicella eruption appeared. The improvement during the incubation period was very striking, 6 lb. being gained in weight; the masses, however, remained; subsequently, the good effect of the varicella proved to be transient and the child lost ground rapidly, the masses increasing in size.

Discussion.—Dr. DONALD PATERSON said that the question had arisen, on the admission of this patient, whether the diagnosis was abdominal tuberculosis, and investigation was carried out from that point of view, but the evidence was in favour of renal sarcoma. The temporary improvement was most interesting, especially in view of statements made by eminent continental scientists that sarcoma cells placed in Ringer's solution into which a certain amount of bleb fluid from chicken-pox was placed, refused to grow. The attack of varicella seemed to have acted in that way in the case of this child.

Dr. F. PARKES WEBER thought that in spite of the "aleukæmic" blood-count, the case would turn out to be allied to leukaemia—namely, a form of "aleukæmic lymphadenosis," if one included under that heading the sarcoma-like forms sometimes distinguished as leukosarcoma and lymphosarcoma. Probably the kidneys and retroperitoneal lymphatic glands were infiltrated, as well as, in a slight degree, the cervical, axillary and inguinal glands. The improvement might be temporary, due to the varicella infection. An important question was whether X-ray treatment in this case was likely to do good or harm.

Dr. DONALD PATERSON (in reply) said he hoped to show the case again in October. If the patient did not survive so long and a post-mortem examination could be made, he would report the findings fully. To those present when the anæsthetic was given there seemed no doubt as to the position and nature of the swelling. It seemed to be separate from the bowel, and to be retroperitoneal, being fastened to the posterior abdominal wall everywhere.

Postscript.—This patient died. At post mortem the diagnosis of renal sarcoma was confirmed.

(?) Case of Kala-azar.

By W. G. WYLLIE, M.D. (for F. J. POYNTON, M.D.).

PATIENT, a girl, aged 5 years, went to Malta when aged one year and eight months and remained there for sixteen months. While in Malta the only complaint she had was an attack of "colitis." About a year after her return to England she was ill for a few days, in March, 1924; there was vomiting and she became slightly jaundiced. She recovered, but in October, 1924, she lost appetite, became sleepy, tired and feverish, and her colour changed to a sallow tint. There was some improvement after three weeks but she has never been really well since, and has been worse since February of this year. The abdomen has been getting larger since December, 1924. The stools have always been well coloured.

On admission to the Children's Hospital, Great Ormond Street, May, 1925, the child showed a moderate degree of emaciation, a sallow colour of the skin, and unusually obvious veins in the abdomen, chest and forehead. The abdomen was large, maximum girth, 22½ in.; lower edge of liver at level of umbilicus; spleen, 3½ finger-breadths below costal margin. Neither the liver nor the spleen felt very hard and did not suggest cirrhosis. A blood-count showed red cells 3,760,000; white 1,560, of which 1,200 were lymphocytes. The Wassermann reaction was negative. Dr. Harrison performed Van den Bergh's test and found a slight

increase of bilirubin in the blood (1 unit), the direct reaction being negative. There were no bile-pigments in the urine. The formol-gel test was strongly positive.

Sir Leonard Rogers examined the case for Dr. Poynton and considered that it was very probably one of kala-azar. Cultures for the organism are being made at present on suitable media.

Discussion.—Dr. F. J. POYNTON said he had thought of such conditions as congenital syphilis, Banti's disease, leukemias, and so on, but he had been struck by the peculiar colour of the patient, and the softness of the liver and spleen. After treating the child with the best preparation of antimony he would report the case again.

Dr. NEILL HOBHOUSE asked whether this case manifested any peculiar type of fever. He had seen cases of this disease in Malta, where it was difficult to distinguish it from acute malaria. A typical feature about kala-azar was that there was a double rise of temperature each day. The infantile form, however, sometimes ran a very benign course, and it was possible that in this case there was scarcely any ascertainable fever.

Dr. POYNTON (in reply) said that this patient's temperature had been mostly normal, but when it did go up there was the tendency to the double phase in the day which Dr. Hobhouse had mentioned. But this would be much more marked in attacks in the adult.

Postscript.—The diagnosis has not yet been entirely confirmed and liver puncture will probably be necessary.

Case of Chorea, with Extensive Vasomotor Disturbance.

By W. G. WYLLIE, M.D. (for R. HUTCHISON, M.D.).

J. E., AGED 10½ years, had an attack of rheumatism twenty-one months ago, associated with chorea. He recovered in four months, but he had a relapse of the chorea four months ago. From the onset of the rheumatic affection his fingers and toes have been persistently blue, and there has been considerable generalized mottling of the skin. There has been no paresthesia, and warmth does not influence the condition. Evidence of a cardiac lesion has never been present.

The systolic blood-pressure is 125 mm. Hg.

Blood calcium and phosphorus are both normal (estimated by Dr. G. A. Harrison).

The Wassermann reaction of the blood is negative.

There is no sign of any angioneurotic condition in the other members of the family.

Case of Chorea, with Extensive Vasomotor Changes.

By W. G. WYLLIE, M.D.

THE main feature of this case is the continuous presence of a deep cyanosis of the toes and fingers during twenty-one months in a boy aged 10 years. It is unaffected by heat; even placing the feet in hot water makes no difference to the appearance. It is somewhat different from the spasmodically dead fingers and toes of Raynaud's disease. The condition arose at the same time as the child developed rheumatism and chorea.

I have not encountered any other cases like it, but Dr. Poynton has described cases of rheumatism in which there were spasmodic affections, such as "dead fingers," muscular spasms and paroxysmal sensory symptoms.

Discussion.—Dr. POYNTON said he had seen one or two remarkable cases of cyanosis after rheumatism, but he did not know why they should occur. These he had described in a paper on "Spasmodic Symptoms in Rheumatism," published in the *Lancet*, October 9, 1915.

Dr. F. PARKES WEBER said the moderate persistent lividity of the feet in this case might perhaps be better termed "acrocyanosis" than Raynaud's disease. There had been no true paroxysms, with pain as well as blueness in the affected extremities, as is characteristic of typical paroxysms of Raynaud's disease.

Section for the Study of Disease in Children.

President—Mr. PHILIP TURNER, M.S.

Case of Giant Nævus.

By J. D. ROLLESTON, M.D.

THE patient is a girl aged 3 years, with a pigmented hairy and warty nævus of "tippet" distribution and numerous accessory nævi. The principal nævus starts in the upper cervical region posteriorly and extends outwards on both sides, involving the posterior aspect of the right shoulder but leaving the left shoulder unaffected, and downwards to the level of the sixth dorsal vertebra.



The pigmentation of the nævus is dark brown interspersed with vitiliginous patches. There are no sensory changes and there is no spina bifida.

The nævus is covered with long downy hairs mostly of a light colour and shows several warty growths of the same colour as the pigmented skin.

In addition to the principal nævus other nævi are scattered over the rest of the skin of the trunk and limbs.

8 Rolleston: *Giant Nævus*; Pritchard: *Abnormal Osteogenesis*

Most of the lesions on the limbs are smooth but a few are hairy. The fewest and smallest lesions are on the face and scalp.

There is no hereditary or familial history of similar lesions, nor is there any history of maternal impressions.

I have brought this case up for two reasons. The first is to ask suggestions in regard to treatment, as a giant nævus is a terrible deformity, especially in the case of a female, and I am most anxious to hear from the surgical and medical members what they would suggest. In the second place a giant nævus is one of the curiosities of medicine, and when it does occur its distribution is usually in the "bathing drawers" area, i.e., the lower part of the back, abdomen, buttocks and the upper third of the thighs. The distribution in the present child is that for which the late Dr. Leonard Guthrie suggested the name "tippet nævus." Eleven years ago¹ I showed before this Section a similar case and one that was even more extensive, and the consensus of opinion then expressed was that it was best not to do anything, because there is always a danger of setting up malignant degeneration. Dr. Poynton, in particular, on that occasion spoke about melanotic sarcoma developing in such cases. I shall be glad to hear what is the opinion on that point to-day.

Another question of some interest is that of maternal impressions. In the last case there was a marked history of maternal impressions, but not in the present case. In the other case, during the third month of pregnancy the mother was frightened by a black dog attempting to bite her husband. She threw her arms over her head and said "I am certain I shall be marked afterwards." Both husband and doctor mocked at the idea, but at the end of term the child was born with a giant nævus. What is the current opinion about maternal impressions? The President of that time, the late Mr. Kellock, expressed his firm belief in their reality and their power to produce nævi. The literature, too, shows there are many who still believe that; even in the Section of Dermatology cases of the kind have been recorded.² There is one rather ingenious theory which was put forward by Bresovsky,³ namely, that for a giant nævus to occur, there must be a twin ovum; that the violent shock produced by the maternal impression causes a reflex contraction of the uterine muscles which breaks up one ovum, and the partially obliterated ovum is transplanted on to the other, so that a person with a giant nævus bears on his surface a portion of his submerged twin brother. I leave you to decide what that theory is worth.

Dr. J. K. BARTON said that if this case were a private patient of his he would take it to the Radium Institute, as the staff there had had such a wide experience of such lesions, and would know what were the dangers of malignant degeneration.

Two Cases of Abnormal Osteogenesis in the Same Family.

By ERIC PRITCHARD, M.D.

THERE is no history of nervous or osteogenetic defect in any other member of the family, but the parents are first cousins once removed. There is one older child, 21 years, healthy, and there was one miscarriage before the birth of the elder of the two patients. There is no evidence of syphilis.

W. S., the elder of the two children, is a girl 17 years of age, her general health is good and she is of more than average intelligence. She appeared healthy at birth and continued so till the age of 1 year when symptoms of general tenderness developed and a diagnosis of infantile scurvy was made. The feeding had been breast (three months) and subsequently "scalded" milk.

Walking was delayed and commenced in a clumsy, ataxic manner at 2 years, but there was much swaying and swinging of the arms to maintain balance. There was

¹ *Proceedings*, 1914, viii (Sect. Dis. Child.), p. 11.

² *Proceedings*, 1911-12, v (Sect. Derm.), pp. 118-119.

³ *Pest. Med.-Chir. Presse*, 1908, xliv, p. 977.

delay and difficulty in starting voluntary movement, somewhat the same as occurs in myotonia congenita (Thomsen's disease).

At 4 years of age the left leg was discovered to be $\frac{1}{4}$ in. shorter than the right. Later, lateral curvature, lordosis and thoracic and pelvic deformity developed, which were appropriately treated by surgical apparatus.

Skiagrams show these deformities with early fusion of the epiphyses. Menstruation commenced early (at 11 years). The disease, which was progressive up to the time of puberty, has since abated.

The patient has been examined from time to time by competent pædiatric, orthopædic and neurological authorities, and the condition has been variously diagnosed as scorbutus at 1 year, rickets at 3 years, thyroid defect at 5 years, pituitary defect at 6 years, progressive muscular atrophy with sclerosis of cord at 7 years, myopathy at 7 years, osteomalacia at 11 years, parathyroid defect at 16 years, and various methods of treatment appropriate to these conditions have been applied without any obvious benefit.

G. S., brother of the foregoing, is 11 years of age. He was born with contractions and flexions of the lower extremities. As these could not be straightened tenotomies were performed and repeated at the ages of 13 months and 5 years. At 6 years of age the same deformities of the spine, thorax and pelvis were noticed as in the case of the girl, and the same delay and difficulty in starting voluntary movements. Fractures took place in the long bones, clavicle and patella. The boy is now in good general health and he can get about by means of two sticks. His intelligence is good. The external genitals are hypoplastic and the testicles undescended.

There is considerable similarity between these two cases, though the girl shows sexual precocity while the boy exhibits rather the reverse. There is no premature fusion of the epiphyses in the boy, but there have been several fractures of bone. Neither case appears to fit in with a progressive muscular atrophy nor with a myopathy.

Although there is in both cases considerable softness or brittleness of bone, in neither case does the skiagraphic picture present the appearance of rickets.

There is no evidence of syphilis, and the fact that there is an older child, 21 years of age, who is healthy, makes familial disease rather doubtful. The blood-pressure has not been tested. The possibility of connexion with pituitary defect is strengthened by X-ray evidence that the pituitary fossa is somewhat enlarged in the girl and somewhat small in the boy.

Discussion.—Dr. F. PARKES WEBER said that an extraordinary developmental disturbance of this kind in brother and sister must be due to some similar endocrine factor at work in both of them. He (the speaker) suggested that in both these patients there was over-action of the suprarenal cortex, accompanied by cortical hyperplasia and possibly by a cortical adenoma. With that view corresponded some of the main features of both cases. First, there was the obesity with hyperæmic face in both brother and sister. Secondly, there was the softness of the bones, a condition that might be associated with hyperplasia or tumour of the suprarenal cortex. He was sorry that the blood-pressure had not been taken; he expected it would be proved to be relatively high in both cases for their ages. But the most important point, in his view, was that, as far as he knew, there was only one endocrine disturbance, which, occurring in early life, might produce smallness of the testicles in the male, and precocious menstruation in the female, namely, an endocrine disturbance connected with hyperplasia or tumour of the suprarenal cortex. One kind of endocrine disturbance might of course be associated with others, and that might be so in the present cases.

Dr. F. J. POYNTON said one of the disturbances with a disorder of bony growth not mentioned was arachnodactylia. He had seen disturbances of the growth of the bones of the pelvis and of the long bones, which were interesting to compare with the cases now brought forward by Dr. Pritchard.

Dr. L. MANDEL said that in both photographs the pelvic deformity was practically the same, and he supposed the gait was identical in both. It would be interesting to know

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whether, when they started to walk, they originally had the same kind of gait. The deformity being on one side only, he gathered, was purely a static result.

Dr. ERIC PRITCHARD (in reply) asked whether Dr. Parkes Weber considered it likely, on the supposition that the cause was a suprarenal condition, especially an adenoma, that the disease would have been arrested. It seemed to him (the speaker) to be a disease of abnormal development, and now that the girl had reached puberty, the process seemed to have come to an end. Both of the children were very intelligent, in spite of their physical disabilities, and the girl was beginning to earn her own living. If the blood-pressure had been high it probably would have produced irritability of disposition; the two children were both very placid and even-tempered. They had been treated in a variety of ways, under the impression that some endocrine defect was present, and for some time interest had centred around the parathyroids. As far as he knew, the treatment by organo-therapy had had no appreciable effect.

Case of Amyotonia Congenita.

By ERIC PRITCHARD, M.D.

H. C., AN infant 3 months old, suffering from symmetrical atrophy and atonicity of muscles since birth. All muscles except those of the face appear to be involved. The intercostal muscles are practically functionless and respiration is almost wholly diaphragmatic. Deep reflexes are absent, but the muscles react feebly to galvanic stimulation. The reaction to faradism is sluggish. The proximal movement of joints is affected more than the peripheral. The wrists and fingers show slight movement, also the toes and ankle-joints. The diagnosis between amyotonia and the spinal type of progressive muscular atrophy (Werdnig-Hoffmann) is open to doubt.

Recently there has been a slight improvement in the movement in the proximal parts of the limbs. It is not a familial condition; it is a purely sporadic case. I should be glad of any suggestion for treatment, electrical or otherwise.

Dr. C. WORSTER-DROUGHT suggested that the case was one of progressive spinal muscular atrophy of Werdnig-Hoffmann type. Apart from the general appearance, the degree of muscular atrophy far outweighed that of the hypotonus. Other features in favour of a diagnosis of progressive muscular atrophy were the tendency to double *main-en-griffe* and the extent of involvement of the intercostal muscles. In amyotonia congenita the intercostals were rarely and very little affected.

Brief Note on a Case of Hemiatrophy in an Infant.

By ERIC PRITCHARD, M.D.

IT is a question whether asymmetrical development on the two sides of the body means hypertrophy of one side or atrophy of the other. This case is that of a child a year old, who was brought to the Infants Hospital in a condition of malnutrition. After it had been in hospital a few days it was noticed that there was asymmetry. This was complete, in that the head, chest and femur were all smaller on the left side. The child had other defects, and subsequently died, and we were unable to secure a post-mortem examination. This child had a curious symptom which may help one to decide whether such cases should be regarded as hemiatrophy or hemi-hypertrophy, namely, that on the atrophied, or smaller, side the child sweated profusely. It sweated a little on the other side, but at times this sweating was completely unilateral on the atrophic side, the line of demarcation being very distinct on the forehead and the chest. Excessive sweating is presumably a pathological symptom, and it would be curious if this pathological symptom should be confined to the normal side.

I had hoped that Mr. Lockhart-Mummery would have been here to defend the other view, namely that the abnormal side is the hypertrophic one. I have had a case like his in which the whole condition has completely disappeared. I saw the case in question fourteen years ago, when the boy was 4 or 5 years of age,

and then there was a considerable difference in the two sides, but at the present time such difference has completely disappeared.

Dr. F. PARKES WEBER considered the difference in the degree of sweating on the two sides was a most valuable observation, as showing that there was a real unilateral disease present, and that the condition was not merely one of asymmetrical development in size—one side of the body growing more rapidly than the other—the asymmetry tending to disappear when the patient becomes older.

Lesion of Mid-brain and Pons.

By N. HOBHOUSE, M.B.

D. H., MALE, aged 3½ years.

Normal during infancy. Said to have been able to walk at 13 or 14 months. Had an illness of some kind at 15 months.

When 17 months old it was noticed that the right eye looked inwards. Shortly afterwards the left arm and leg became weak; at 2 years old he could no longer walk and scarcely used the left arm.

Present state.—Complete paralysis of both external recti. Defective upward movement of the eyeballs. Nystagmoid jerkings on attempted movement. Considerable weakness of right facial muscles, including orbicularis. Dribbling, difficulty in swallowing, very little attempt at talking. Fundi and discs normal.

Spastic paresis of left arm and leg; increased tendon-jerks and extensor plantar response. No sensory change detected.

Wassermann reaction of cerebro-spinal fluid negative.

The child has been under periodic observation since June, and the condition appears to be slowly progressive; the weakness and stiffness of the leg have increased, and there is more difficulty in swallowing.

The diagnosis appears to lie between tumour and encephalitis.

Dr. C. WORSTER-DROUGHT said he thought the diagnosis was more likely to be encephalitis lethargica. A two years' history was rather a long one for a cerebral tumour in a child, and the absence of other manifestations—fundus changes, convulsive attacks, &c.—was also against this diagnosis. A further point in favour of encephalitis lethargica was the presence of Parinaud's syndrome—the inability to rotate the eyeballs upwards—which so frequently occurred in this disease. He had seen several cases of undoubted encephalitis lethargica in which Parkinsonism existed with hemiplegia of pyramidal type.

A Case of Hirschsprung's Disease with Optic Atrophy and Old Choroiditis.

By C. WORSTER-DROUGHT, M.D.

L. K., AGED 8 years. This child first came under observation at the age of five, with the complaint that her vision was defective and that she was restless and tended to adopt faulty postures. The eye condition and slight scoliosis were noted, and at that time there was no complaint of abdominal trouble. She had had no previous illnesses but her father says that he noticed oscillation of the eyes shortly after birth.

In July, 1924, the child was again seen, her parents stating that for the past six months her abdomen had been noticed to be very large each evening; the swelling would disappear during the night, but re-accumulated during the day. Also, she had lost much flesh in spite of a ravenous appetite. There was no history of constipation, but she had occasional diarrhoea.

On examination, the abdomen was found to be unduly distended and expanding the costal margins. On percussion, the note was tympanitic throughout, the liver

dullness being abolished; there were no palpable masses and no tender points. Digital examination of the rectum showed some spasm of the internal sphincter. In hospital she was observed to pass much flatus during the night.

An X-ray examination following a barium enema showed the entire colon to be enormously dilated (*vide* photograph); this was also confirmed by the ordinary barium meal by the mouth (Dr. Martin Berry).

The child is poorly nourished and somewhat mentally backward. There is left internal strabismus with error of refraction of 6 D. hypermetropia. The right



Skiagram taken after a barium enema showing the dilated colon (Dr. Martin Berry).

eye has a small anterior polar cataract. Each fundus shows optic atrophy with a degenerated retina and old choroiditis. Apart from the eye condition, the nervous system shows no abnormality.

The blood and cerebro-spinal fluid both yield a negative Wassermann reaction and the latter is normal in all respects (cells, protein and colloidal gold curve).

I have never before seen a case of Hirschsprung's disease associated with optic atrophy, nor have I heard of such an occurrence; possibly the association is purely accidental. The case strongly supports the view that Hirschsprung's disease is not congenital, and also indicates that constipation is by no means a necessary symptom.

The aetiology of the optic atrophy and choroiditis is obscure. Congenital syphilis has been considered, but the presence of a negative Wassermann reaction in the patient's blood and cerebro-spinal fluid, as well as in the blood of both parents, would appear to exclude this disease.

Discussion.—Dr. F. PARKES WEBER said he did not agree that the connexion between the eye condition and Hirschsprung's disease was a merely casual one. Hirschsprung's disease (congenital megalocolon) indicated a congenital abnormality of development. When one congenital developmental abnormality was present a search sometimes showed that others existed in the same patient, for instance, a congenital abnormality of the heart. In the present case the ocular abnormality was certainly in part, if not altogether, of congenital origin. He compared the association of congenital megalocolon with congenital abnormalities of the heart or eye to the well-known occasional association of "mongolism" with congenital abnormalities of the heart, &c.

Dr. C. WORSTER-DROUGHT (in reply) expressed his agreement with Dr. Parkes Weber's remarks. He had made a fairly exhaustive search in the literature and had not found optic atrophy mentioned in connexion with Hirschsprung's disease; therefore, he had thought that the association in this case was possibly accidental.

Case of Incoördination—Probable Astatic-Hypotonic Form of Cerebral Diplegia.

Shown by Dr. E. W. FULTON (for C. WORSTER-DROUGHT, M.D.).

J. B., FEMALE, aged 2 years 9 months on admission to hospital on April 3, 1925, as "unable to walk or talk." Delivery was normal, and she sat up when 14 months old and walked with help at 2 years. Dentition not delayed; sphincter control since age of 28 months. For a few months preceding admission her attempts at walking deteriorated. The child has always been contented and otherwise healthy. There is nothing of importance in the family history, there being one elder sister, aged 6, who is quite normal.

Physical examination.—Frontal bone highly arched and nasal bridge somewhat depressed. Pupils normal, optic discs pale (due to lack of pigment), left internal strabismus, no nystagmus. Sensation normal. All movements present in limbs, the legs show slight hypotonia; the arm-, knee- and ankle-jerks and abdominal reflexes are all normal. *Gait.*—On admission to hospital she could stand only when supported, but with treatment by means of walking exercises, &c., she is able to walk a little with assistance, but the gait remains stiff and awkward on rather a wide base, with a tendency to throw the right leg outwards. Unassisted, she staggers and falls. The legs show gross ataxia, and the arms a certain amount—as seen when the patient is attempting to feed herself, &c. All other organs are normal.

Mentality.—She appears to understand all that is said to her and obeys simple commands as far as the ataxia permits. She is inclined to be obstinate, but is neither vindictive nor emotional. Habits quite clean. Speech is monosyllabic only, and articulation indistinct.

On April 21 the blood was reported as yielding a weak, partial positive Wassermann reaction: cerebro-spinal fluid, doubtful Wassermann reaction. The cells and protein content in the latter, however, were normal. Later tests have invariably yielded a negative Wassermann reaction, both in blood and cerebro-spinal fluid—even after a "provocative" dose of sulfarsenol. The colloidal-gold reaction in the cerebro-spinal fluid was negative throughout.

It is suggested that this case is one of the group of so-called "cerebral diplegias" (Little's disease), but instead of the more usual involvement of the cerebral (or pyramidal) system the cerebellar neurones are affected by the degeneration.

Anglade and Jacquin (1909) have recorded a case of cerebral diplegia, with autopsy, in which a neuronie degeneration of the cerebellar cortex was found, in

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addition to a similar condition in the cerebrum. F. E. Batten also reported examples of an astatic-hypotonic type of diplegia and considered that the cerebellum was extensively involved (J. S. Collier).

Dr. F. PARKES WEBER said he considered that the case belonged to the group of familial ataxies, although in this particular case no familial history of any similar condition was forthcoming. Dr. F. E. Batten first brought forward such cases under the heading, familial or congenital (cerebellar) ataxy. In reality such cases were of the nature of a diplegia in which the cerebellum was particularly involved, as suggested by Dr. Fulton.

Case of *Granuloma Annulare*.

By HUGH THURSFIELD, M.D. (shown by Dr. K. TALLERMAN, M.C.).

THE patient, I. W., is a girl aged $3\frac{1}{2}$ years. There is a family history of rheumatism, none of tuberculosis. The patient herself has no past history of any disease but measles. Five months ago, a small subcutaneous swelling was noted on the child's right knee. A little later, similar nodules were noted on the front of the legs, the arms and elbows. On admission to hospital, nodules were noted lying subcutaneously over the left tibia. Over the right knee was a firm swelling with shotty nodules in it. Nodules were noted over the right elbow, and along the forearm were two nodules the size of peas, and others were seen on the dorsum of the left foot. These nodules were not tender, appeared hard, were fairly movable and varied in size. The child appeared quite healthy. A week after admission all the subcutaneous nodules except those over the right elbow and left tibia had disappeared. An oval ring of intracutaneous nodules appeared, however, on the dorsum of the left foot. These were raised, not tender, and varied in size from that of a pin's head to that of a small pea. Subsequently, other small intracutaneous nodules have appeared on the sole of the right foot and on the left foot. Von Pirquet reaction negative. No reaction to subcutaneous injection of 0.001 grm. O.T.

One of the intracutaneous nodules was examined; the section shows marked fibrosis with the presence of some large multinucleated cells, and inflammatory reaction, especially around some of the small vessels and nerves.

Case of Congenital Diaphragmatic Hernia.

By HUGH THURSFIELD, M.D. (shown by Dr. K. TALLERMAN, M.C.).

J. L., A MALE child, aged 6 months, was brought to hospital on account of shortness of breath and loss of weight.

The family history is completely negative. Birth weight $7\frac{3}{4}$ lb. The child is breast-fed. For the last three months the mother has noted that he has attacks of moaning accompanied by shortness of breath. His bowels are normal and he has vomited only occasionally. He takes his food well, is not restless and sleeps soundly. On admission he seemed perfectly well except that his respiration at times appeared embarrassed.

This dyspnoea has become worse, is present now most of the day, and bad attacks occur from time to time after feeding. During such attacks the infant cries, appears to be in pain, and relief is only afforded by laying him face downwards. Cyanosis has been noticed at times.

Physical Examination.—The percussion note and breath sounds are normal over the right side of the chest. On the left anteriorly, the note over the apex is impaired, below this it is hyper-resonant although it varies from time to time. Except at the apex, where the breath sounds are diminished, the breath sounds are absent and gurgling noises are heard. Posteriorly, the percussion note is impaired and the breath sounds absent throughout. The area of cardiac dullness cannot be well

defined and the apex beat is not palpable. No heart sounds are heard to the left of the sternum. To the right they are best heard about 1 in. from the mid-sternal line in the second and third interspaces.

In the abdomen a rounded mass can be felt in the mid-abdominal plane just to the left of the mid-line. It is about 2 in. long and $1\frac{1}{2}$ in. across. It is freely movable on palpation but not on respiration. The percussion note over it is dull.

The liver appears to lie obliquely, extending across the right side of the abdomen and almost down to the umbilicus.

Another less easily definable mass, rather soft and more deeply placed, can be felt in the right hypochondriac region and extending down to the right iliac fossa.

The X-ray findings are as follows:—

Heart displaced to the right, gas-filled viscera extending high up in the left hemithorax.

Subsequent to an Opaque Meal:—Meal passes normally through the œsophagus. The stomach lies apparently in the pelvis and is dilated and large. It is rotated, the pylorus being on the left side. From the outset, food passes into the small intestine situated in the thorax. Stomach empties at the normal rate. In six hours the meal is all in the colon; it is difficult to say which portion of colon, except that a single loop continuous with rectum is filled, so it is presumed to be splenic flexure, descending and pelvic colon.

Following an opaque enema the colon is seen to be completely filled, and the appearance suggests that the cæcum and transverse colon are in the thorax.

Mr. PHILIP TURNER (President) said this was a very interesting and remarkable case, and on looking at the child and reading the account one wondered what the diagnosis would have been without the assistance of the X-rays. He mentioned that, because this was like a case he saw about twenty years ago, an infant of about the same age, under the care of Dr. Cautley at the Belgrave Hospital. The symptoms seemed to have been very similar in the two cases. At the date of which he spoke, bismuth and X-ray examinations were scarcely ever made, certainly not in the case of infants. In that case the conclusion was that the child possibly had an empyema. It was given an anæsthetic and an exploration was made with the needle in various directions, in search for pus, but none was found; the case was a most mysterious one. At the post-mortem examination it was a surprise to find that in the thorax, on the left side, there was stomach and liver, as well as intestine.

With regard to surgical treatment, he did not know of any of these cases in children in which operation had been done; in adults there had been a few operations after rupture of the diaphragm. In such cases he thought it was necessary to approach the diaphragm from above, doing a transpleural operation. In the case of a child he doubted whether any operative procedure was possible. If any Member had heard of such a case in a child having been operated upon, he (the President) hoped that he would mention it.

Case of Failure of Ossification and other Abnormalities of Bones.

By DONALD PATERSON, M.B.

FEMALE, aged $5\frac{1}{2}$ years. Since birth slight abnormalities of the face and skull have been noted. Her face is flat and the bridge of the nose sunken. The cheeks are prominent and the eyes slightly slanting like those of a mongol. The head is set down between the shoulders.

There are two other members of the family (boys) who are quite normal in every way. The mother and father appear quite normal. The Wassermann reaction is negative in both mother and child. At 22 months of age the child was noticed to have bony deformities resembling rickets and was brought under observation. X-ray examination showed slight rickets, but the outstanding changes were the fact that the heads of the femora appeared entirely absent. The carpal bones were late in

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appearing. The child was unable to close her hands completely. There was well-marked genu valgum. She was undersized for her age.

From this time till the present—a period of $3\frac{1}{4}$ years—the child has been under observation and treatment. She has remained undersized although mentally she is quite normal. The same abnormalities exist. The X-ray appearance has altered very little indeed, although a slight attempt at ossification can be seen in the necks of the femora, but the heads are still entirely absent.



Note.—The centre of ossification of the femora is entirely absent.

Throughout this period she has had cod-liver oil. She has been exposed to much sunshine and has undergone massage; thyroid, parathyroid, pituitary and mixed gland preparations, calcium lactate, and other calcium salts, have been given. There is no reason to believe that any of these things have benefited the child in the least. Her urinary examination proved negative, and an examination of her other systems shows them to be normal.

I think there has been only one other case of the kind shown, and that was exhibited by Dr. Thursfield, at the Section of Orthopædics.¹ He will now perhaps show a skiagram of that also.

Discussion.—Dr. HUGH THURSFIELD said that Dr. Paterson's patient was in personal appearance the image of his own patient. (Epidiastroscope demonstration.) The bony changes all over the body were, in his experience, unique. Practically every bone in the boy's body showed the same kind of defective ossification, and these two cases appeared to form a completely new class of congenital or very early bone disease. He did not think it was necessary to invoke endocrine defect in explanation of all these abnormalities. Dr. Poynton, in the discussion on another case, referred to another abnormality, arachnodactylia, which was

¹ *Proceedings*, 1925, xviii (Sect. Orth.), p. 42.

also a mysterious condition. A third condition had been shown at this Section once only. Obviously there were many bony defects, originating in early life, which the medical profession had not yet begun to understand. When there was recognized endocrine defect bony deformities were occasionally present, but in most cases the bones were fairly normal. He suggested classifying these cases simply as bony defects, and leaving any hypothesis as to their causation for future consideration. To his mind this case of Dr. Paterson's and his own case were more nearly allied to chondro-dystrophia than to any other disorder.

Dr. F. PARKES WEBER said he did not think there was any reason or basis for regarding such cases as due to endocrine defect. The cranio-facial developmental abnormality in the case was probably a minor degree of what David Greig termed "hypertelorism," a kind of "cranio-facial dysostosis."

Case of Swelling of the Knees probably due to the Toxins of Tuberculosis.

By DONALD PATERSON, M.B.

G. F., MALE, aged 4 years. A year ago the child fell on his knees. There was some swelling which rapidly disappeared. Since then this has reappeared from time to time. The swelling has been greater in the morning and less in the evening. It is not painful. Rest appears to help it, but does not cause a complete disappearance. Exercise is difficult because of the size of the knees, but not painful.

The child's father died about a year ago, at the time that the first swelling appeared. He suffered from pulmonary tuberculosis. The child was in contact with him. An X-ray of the patient's chest shows a calcified area just to the left of the mediastinum the size of a two-shilling piece. The von Pirquet test is strongly positive to the human and moderately positive to the bovine. The blood-count is normal. The Wassermann reaction is negative.

I suggest that the swellings were primarily traumatic in origin, but have been maintained by the presence of healing tuberculosis in the child, as I can find no other focus of infection.

Case of Enlarged Thymus, with Stridor and Tetany.

By LEOPOLD MANDEL, M.D.

PATIENT, a boy, R. M., when aged 10 weeks, weighed 12 lb. 12 oz., and was brought to my out-patient department on September 15, 1925, with a history of noisy breathing since birth, accompanied by slight fits or convulsions, during which he "turned blue."

Family History: Good on both sides. Parents (first cousins) have been married ten years. Patient is the third child; other children normal.

Patient was a full-time child; labour was normal; the child is breast-fed. Mother noticed that breathing was harsh from birth, but became distinctly "croaky" when the infant was 14 days old; shortly after this the first fit occurred, a second fit occurred in the third week and three further fits during the fourth, seventh, and tenth weeks. I saw this last "fit" myself. It was tetany; the spasm was bilateral and symmetrical, and both upper and lower extremities were implicated, the hands more than the feet. The spasm lasted only about half an hour. After the spasm and for some fourteen days further Trousseau's sign was positive, but I was never certain of Chvostek's sign. The temperature rose to 99° 8' F.; there was no vomiting, diarrhoea, or laryngospasm; the face was rather livid and the lips were blue. The breathing was regular, but very noisy; there was a distinct stridor, harsh, but not whistling in type.

The infant was examined under an anæsthetic a week later by Mr. H. Kisch, who reported "epiglottis normal, but adenoids present."

Percussion gave a suggestion of increased dullness in the suprasternal region, and an X-ray examination was made by Captain A. Marsh, who reported: "Half-tone shadows both sides of neck extending above clavicle, and they can be traced down to pericardium. The whole area of shadow represents the appearance of an enlarged thymus." This X-ray photograph was taken when the child was 13 weeks old.

The features interesting to my mind are (1) the apparently extraordinarily enlarged thymus (it is difficult to say what else the shadow can be); (2) the tetany in a breast-fed infant at such an early age, and (3) the congenital stridor which cannot, as is usual, be explained by an abnormal epiglottis, nor entirely by the adenoids. Another interesting point is that the mother thought the infant was temporarily blind after the administration of the anæsthetic.

The child has undoubtedly improved; it is still on the breast; it now weighs 14 lb. and has had no recurrence of the tetany. I intend to treat it with X-rays—say quarter-pastille. Possibly the actual taking of the photograph has already improved the condition, for in Germany I understand that these cases of enlarged thymus are treated by X-ray therapy.

Discussion.—Dr. HUGH THURSFIELD said that many years ago Kops had described asthmatic attacks arising in infants owing to the presence of an unduly large thymus gland. Friedleben, after investigating the matter for many years, concluded that there was no such thing. There the matter rested for some thirty years. Then the French and the Americans, simultaneously, started the same story again. A study of the French literature on the subject compelled acceptance of the conclusion that such a condition did exist, but that it must be extraordinarily rare. He had had six or more cases in which the question had been raised, and in every one of these cases it was found, in the event, that the thymus gland was not at fault.

As to X-ray diagnosis of enlargement of the thymus, he was completely sceptical. The fact was that these children who had asthmatic attacks, with impaired percussion note and stridor, usually turned out to be either cases of septic glands arising from the throat,—glands which were deep in the neck, beneath the deep cervical fascia, pressing upon, and sometimes distorting, the trachea,—or, more commonly, they were tuberculous glands, and when that was so, there was but little hope for the patient, as, at that age, tuberculosis of the glands was almost as fatal as any other form of tuberculosis. A case which for some time he thought was an enlarged thymus was that of a child who had all the alleged symptoms of enlarged thymus, but just as the question of the propriety of opening the thorax was being considered, a red spot appeared above the clavicle, followed by the discharge of a fair quantity of pneumococcus pus. The thymus shadow, so-called, then disappeared, and the child got well. The Americans had reported fifty to sixty cases of operation on supposed cases of enlarged thymus, and in the majority of the post-mortem records on them there was sepsis in and about the neck.

Dr. ERIC PRITCHARD asked whether there were any symptoms of status lymphaticus during the administration of the anæsthetic.

Dr. MANDEL (in reply) said that the diagnosis of enlarged thymus had not then been made, and he thought it was an ordinary laryngeal stridor; chloroform was given unwittingly, and there was no bad effect from it. The only bad event was the story of temporary blindness related by the mother, and he (Dr. Mandel) believed that such had been recorded in association with ethyl chloride administration.

Section for the Study of Disease in Children.

President—Mr. PHILIP TURNER, M.S.

DISCUSSION ON THE DIAGNOSIS AND TREATMENT OF SPLENIC ENLARGEMENT IN CHILDREN.

Sir HUMPHRY ROLLESTON, Bt., K.C.B., P.R.C.P.

INTRODUCTORY.

ENLARGEMENT of the spleen is a physical sign, like jaundice, due to many causes, which in the vast majority of cases are infective, though in many instances, such as in von Jaksch's anaemia and aplastic anaemia, it may be impossible to go further than to assume such an origin. The more unstable condition, as regards response to stimulation, of the blood-forming organs in early life as compared with that in adult life makes the significance of the blood-picture a difficult and therefore an interesting problem.

The spleen and the lymphadenoid tissues generally are more prone to active response and enlargement in childhood than in later life, and the spleen in particular is more distensible than in adults. In considering the subject it will be well to take conditions in which the spleen is very definitely enlarged, and not to include cases in early infancy in which the edge can be felt just below the ribs; this is of less significance in early infancy than in subsequent years. In G. Carpenter's series of 348 cases of enlarged spleen in children under 12 years of age, 94 occurred in the first six months of life and 220 under 18 months of age; it is probable that some of these were due to rickety deformity displacing the spleen downwards, rather than to real splenomegaly.

A special point of interest in connexion with splenic enlargement is in the early stages of the chronic diseases in which it is recognized as occurring, when the other manifestations characteristic of the fully developed disease have not appeared. In some instances splenomegaly may constitute the chief or only clinical sign of an incomplete or *fruste* form of a disease—for example, in chronic hæmolytic jaundice and Hanot's cirrhosis. A palpable spleen has been found as the only physical sign in a family in which other members had Hanot's hypertrophic biliary cirrhosis (Boinet).

A question deserving discussion is the probability that in some cases splenic enlargement is due to more than one factor—for example, syphilis complicated by a low grade streptococcal infection or by tuberculosis. Syphilis may well favour a secondary infection, and then (*vide infra*) anti-syphilitic treatment may fail to be curative.

It would no doubt be convenient to group the forms of splenomegaly under a number of inclusive headings, such as (1) those that may be familial (chronic splenomegalic hæmolytic jaundice, Gaucher's disease, and congenital syphilis); (2) those associated with changes in the blood-picture (anaemia, hæmolysis, erythræmia, leukaemia); (3) those definitely infective, whether acute, as in enteric fever, or chronic as in congenital syphilis and tuberculosis; (4) those of tropical origin (malaria, kala-azar); (5) mechanical (growths, cysts, infarcts); (6) associated with hepatic enlargement or cirrhosis. But though this arrangement is attempted, there is obviously such an amount of overlapping as to render it of little value, except as a means of arranging the various conditions in some order or other.

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(1) FAMILIAL SPLENOMEGALY.

Familial splenomegaly may be due to chronic splenomegalic hæmolytic jaundice, Gaucher's disease, and congenital syphilis. In addition, it is well to bear in mind the possibility that familial splenomegaly may occur in other and undetermined conditions; De Lange and Schippers recorded a family of seven in which four children had enlarged spleens; one died from hæmatemesis and two others underwent splenectomy.

In chronic splenomegalic hæmolytic jaundice the diagnosis depends on the examination of the blood for fragility of the red cells; and the treatment, in cases with symptoms demanding it, is splenectomy. After splenectomy the symptoms of chronic hæmolytic jaundice disappear, but the red blood-cells hardly ever become normal as regards fragility, thus suggesting that the fragility is an inherent peculiarity. So far this fits in with Naegeli's suggestion that the microcytosis of the condition is evidence that these patients belong to a different type of human species. But against this interesting conception are the observations that microcytosis is confined to those members of a family with chronic hæmolytic jaundice (Meulengrath), and that after splenectomy microcytosis diminishes (Whitcher).

The cholesterol content of the blood rises after splenectomy, and this might suggest that the fragility and hæmolysis depend on the low cholesterol content; but an equally low content is found in some anæmias without fragility (Campbell and Warner), and it has been thought to depend on the relative proportions of cholesterol and lecithin. Thus the medicinal administration of cholesterol in chronic hæmolytic jaundice does not rest on such a logical basis as might have appeared at first. X-ray exposures were recommended by Parisot and Heully as the result of benefit in two cases of the congenital form, but subsequent experience does not appear to have been confirmatory.

Gaucher's Disease.

This condition (*épithéliome primitif*), first described in 1882 as a neoplasm, is now considered to be a special change in the reticulo-endothelial system, and from its racial (Jewish), familial, sexual, and congenital characters has been regarded as a constitutional anomaly, a mutation in the human species (Naegeli; Waugh and MacIntosh). It is a striking but rare disease; in 1924 Conner referred to twenty-four recorded cases. It is familial, but this has not always been established—for instance, the sixth recorded case in France was the first shown to be familial (Harvier and Lebée). Though the condition involves the spleen, lymphatic glands, liver, and bone marrow probably simultaneously, it is most obvious, both in point of its chronological appearance and objectively, in the spleen, which may be larger than in any other disease suitable for splenectomy; the superficial lymphatic glands are very seldom enlarged. From the distribution of the lesion splenectomy cannot be expected to bring about a real cure, but it gives relief. In Harvier and Lebée's 13 collected cases of splenectomy (9 adults, 4 children) there were 3 deaths after operation, and among 51 collected splenectomies in patients under the age of 14 years 4 were for this condition (Bartlett). It is characterized by a peculiar yellowish wedge-shaped thickening of the conjunctivæ, commonly seen on both sides of the cornea. According to Brill and Mandlebaum, the skin, though showing a peculiar brownish-yellow discoloration in areas exposed to the light, is never jaundiced. Now as the reticulo-endothelial system is concerned with the formation of bilirubin out of hæmoglobin, the interesting question arises whether jaundice can occur in Gaucher's disease; observations with Hijmans van den Bergh's test should throw light on this point. It is noteworthy that in Willmore and Mackenzie Douglas's case of an adrenal tumour with extensive degeneration of the reticulo-endothelial system anæmia and jaundice were absent.

Splenic Enlargement in Congenital Syphilis.

This was first pointed out, at any rate in this country, by Gee in a paper read before, but not deemed worthy of inclusion in the *Transactions* of, the Royal Medical and Chirurgical Society. Gee found it in 25 per cent. of his cases, Still in 45 per cent., Marfan in 50 per cent., and Coutts in 63 per cent. It is an index of the severity and activity of the infection; in infants born with syphilitic manifestations it is almost always enlarged; in cases in which they appear later the spleen may enlarge before they become obvious, but usually this sequence is reversed; hence the variations in statistics may be explained.

In older children splenic enlargement associated with anæmia should always suggest syphilitic infection and the Wassermann or the therapeutic test should be carried out. The imitation of splenic anæmia and the further stage of Banti's disease by delayed congenital syphilis is well known.

In children with an enlarged spleen and a positive Wassermann reaction anti-syphilitic treatment may be disappointing, and there may not be any improvement until splenectomy has been performed. Farley has collected seven cases, not including Weil's, but all except French and Turner's were in adults. In such a case, reported by Osman, failure of salvarsan led to splenectomy, when the liver was seen to be cirrhotic; this was followed by apparent cure with a negative Wassermann reaction for six years, when hæmatemesis and cerebral symptoms proved fatal. The patient of French and Turner, a boy aged 5 years, in whom the blood-picture had previously been that of von Jaksch's anæmia pseudo-leukæmica infantum, was very similar, except that cirrhosis was not recorded and that a younger sister also had splenomegaly.

The interesting question arises why antisyphilitic treatment fails to exert a curative action; Weil, indeed, suggested that the Wassermann reaction was due to an unknown parasite, but perhaps the more probable view is that syphilitic infection had been complicated by a secondary infection in the spleen, like that presumed to be responsible for the chronic splenic anæmia of adults.

(2) CASES ASSOCIATED WITH CHANGES IN THE BLOOD-PICTURE.

Acute Leukæmia.

In early life acute leukæmia is probably more often of the myeloid or myeloblastic than of the lymphoid type; it should be recognized by the blood examination. If acute progress occurs in cases previously latent the spleen may reach a large size. Except in the rare cases, such as those of Cabot, Marchand, and Arthur Hall, which turn out to be examples of the lymphocytosis of acute infection,¹ and thus imitate acute lymphoid leukæmia, the prognosis is hopeless, and treatment with benzol, radium, X-rays, and arsenic fails even to retard the inevitable end. Splenectomy, which W. J. Mayo carried out after preliminary X-ray exposures in thirty-one cases, with beneficial results in more than a third of the patients, does not appear to be suited to the acute cases in early life.

Murray H. Bass has recorded unusual eosinophilia with splenomegaly in a girl aged 6 years belonging to the small group of cases in the adult called eosinophilic leukæmia; the white count (25,600) showed 37 to 64 per cent. of eosinophils, with 6 per cent. of eosinophil myelocytes.

Pernicious Anæmia.

Pernicious anæmia is very rare in early life, but aplastic anæmia occurs, and from examination of a blood-film only may suggest acute lymphoid leukæmia or the existence of the rather discredited entity leukanæmia.

¹ H. L. Tidy, it may be mentioned, has vigorously criticized the existence of cases of absolute lymphocytosis due to sepsis.

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Thrombocytopenic Purpura Hæmorrhagica.

This may be (a) primary and constitutional, or (b) secondary to infection, such as by *Streptococcus hæmolyticus*, to drug poisoning (such as benzol), and to morbid conditions such as nephritis, hepatic cirrhosis, and leukæmia. It may be acute and even fulminating, or chronic and recur for years. It is characterized by a diminution in the number of the blood-platelets, from the normal 250,000 to 40,000, 5,000, or lower, a normal coagulation time and a prolonged bleeding time often exceeding two hours (Dukes), and in the active stage by some enlargement of the spleen. There are various views as to the evil influence of the spleen in this condition, and as to the mechanism of the good results of splenectomy introduced by Frank of Breslau in 1915, and followed by Kaznelson of Prague (1917), Brill and Rosenthal (1923) in New York, B. Vincent (1925) in Boston, Cowen (1925) in Australia, and Sutherland and Williamson (1925) in London. Ricaldo and Albo report cures by splenectomy of chronic hæmorrhagic purpura without splenomegaly. Frank suggested that the spleen inhibited the activity of the bone marrow; Kaznelson that it removed platelets from the blood; and Brill and Rosenthal that it produced a toxin.

Acute thrombocytopenic purpura hæmorrhagica can be distinguished from acute lymphoid leukæmia and aplastic anæmia by the blood-count; from the hæmorrhagic forms of diphtheria and the exanthemata by careful examination; from scurvy by the history, the spongy gums, and the reaction to antiscorbutic remedies. The chronic form can be differentiated from hæmophilia by the absence of superficial hæmorrhages, the normal platelet count, and the normal bleeding time in the hereditary disease.

In the past the chief form of treatment was transfusion, which had sometimes to be repeated. Splenectomy can now be employed as an emergency measure in acute cases when other means have failed to arrest the bleeding, and in the chronic form is regarded as the best remedy by Vincent, who found five fatal cases in almost fifty collected cases of the disease treated by splenectomy.

Infantile Splenic Anæmia.

Infantile splenic anæmia, meaning thereby von Jaksch's anæmia pseudo-leukæmica infantum (1889), also described by Luzet (1891), whose name is bracketed with von Jaksch's by the French, and also called splenomegaly with anæmia and myelæmia, should be definitely separated from the juvenile form of chronic splenic anæmia of adults, and for this reason von Jaksch's more cumbersome title perhaps has an advantage. It appears, like chlorosis, to have become rarer in recent years (Thomson). It is confined to the first three years of life, its maximum incidence falling in the middle of this period, and is characterized by great splenic enlargement, secondary anæmia with leucocytosis (30,000), some relative lymphocytic increase, the presence of nucleated reds, a constant myelæmia (up to 6 per cent.), and tendency to spontaneous recovery. It is often associated with rickets; but, except for Beretervide and Bianchi, modern writers do not consider that congenital syphilis, which certainly is found in a proportion (less than half) of the cases, is responsible except by diminishing the resistance to the as yet unknown cause. Marquard recorded the disease in twins, and suggested that some congenital factor is responsible, but the tendency to spontaneous recovery is rather against this view. Thursfield, who has paid special attention to this disease during this century, puts the recovery rate at 65 to 70 per cent., and doubts the suggestion that it is specially frequent in Jews. It is familial; the twins figuring in the frontispiece of Hutchison's "Lectures on Children's Diseases," when seen at the age of 12 years, had recovered and their spleens were no longer palpable; but splenic enlargement may persist after the blood-picture has become normal. Beretervide and Bianchi, of Buenos Aires, also differ from the general opinion in taking a gloomy prognostic view, and state that in ten years' experience they have not seen a cure; the possibility that the disease they

describe is different from the British form in some respects, ætiologically or environmentally, naturally arises. In the absence of any definite knowledge of its real cause reliance has chiefly been placed on hygienic measures; splenectomy, which would seem rather unnecessary in the light of the recovery rate, has, according to Bartlett, been carried out in five cases.

Chronic Splenic Anæmia.

That chronic splenic anæmia of the form seen in adults may occur in older children I have no doubt. There is rightly some scepticism about the existence of such a condition, and it may fairly be said that it is only cases of unknown origin which can be so labelled. But there are such cases which cannot, in the presence of a negative Wassermann reaction, be regarded as syphilitic, unless the view be taken that the splenomegaly is the legacy of a spirochætal infection which has died out. Some young adults with chronic splenic anæmia have had an enlarged spleen from childhood; I have recorded such a case, and Leech reported a case fatal after splenectomy (spleen 426 grm., or 13 oz.) in a boy aged 9 years with a negative Wassermann reaction. It has been suggested that von Jaksch's anæmia is the infantile form of the chronic splenic anæmia of adults, and that the blood-picture depends on the more active response of the blood-forming organs; but the difference in the prognosis—von Jaksch's anæmia often undergoing spontaneous cure, while chronic splenic anæmia of adults does not—makes this an improbable assumption. I have not any reference to chronic splenic anæmia due to thrombosis of the splenic vein in a child.

Banti's Disease.

In Banti's disease and portal cirrhosis with splenomegaly, removal of the spleen has sometimes been beneficial (Osman), but the general opinion is that splenectomy is most successful in cases before the liver has become cirrhotic—namely, in the stage corresponding to splenic anæmia and before Banti's disease has supervened. Among 69 collected cases of splenectomy for chronic splenic anæmia—mainly in adults as shown by the average age of 33 years, the extremes being 2½ and 69 years—Chaney found that 23·3 per cent. of the 30 cases showing hepatic cirrhosis proved fatal within forty days of the operation, whereas in cases without hepatic cirrhosis the corresponding mortality was 13 per cent. Richards and Day found that in Egyptian splenomegaly, in which hepatic cirrhosis is an early accompaniment, splenectomy was beneficial if performed before the appearance of ascites.

Erythræmia.

The spleen is nearly always enlarged in this condition, which, however, is rare in childhood. In his monograph on the subject Parkes Weber refers to about six cases in early life, two of which were probably associated with congenital syphilis. Poynton, Thursfield, and Paterson recorded a case in a girl aged 3½ years. Splenectomy is inadvisable, as the spleen serves as an overflow for the excess of blood. Benzol by the mouth and X-ray exposures of the long bones may be tried, and the question of intestinal infection and toxæmia should be considered.

(3) CASES OF INFECTIVE ORIGIN.

Infective Splenomegaly.

Infective splenomegaly as part of an acute general affection of the hæmopoietic system is very rare. I have seen a mixed infection of the glands, which in places were breaking down, due to *Bacillus coli* and streptococci. Osman reported a case of anæmia with splenomegaly associated with tonsillitis in a boy aged 6½ years who was in good health eight years later. Infarcts and enlargement of the spleen in

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malignant endocarditis, and the spleen of enteric fever, should be recognized by the special features of the causal disease.

As regards chronic infections, the field is large. Perhaps the palpable spleen sometimes present in status lymphaticus may, like that condition, be due to a low-grade infection, as suggested by H. C. Cameron. In Still's disease, or the juvenile form of rheumatoid (chronic infective) arthritis, the spleen and lymphatic glands are enlarged, and amyloid change has been reported.

Tuberculosis of the Spleen.

Tuberculosis may give rise to very considerable enlargement, both in acute miliary tuberculosis and in the chronic form. In chronic tuberculosis the organ may contain comparatively large caseous masses, resembling to the naked-eye lymphadenoma. There may be adhesions to the diaphragm, so that the organ, though increased in size, cannot be felt. Owing to the perisplenitis there may be pain and tenderness, and Thursfield considers that tuberculosis is the only condition of the organ in which it is often distinctly tender.

Lymphadenoma.

This is not uncommon in older children, but it is very rare to find it predominantly splenic as in a boy aged 11 years, recorded by Poynton, Thursfield, and Paterson; in this case the spleen weighed 25 oz., the liver 44 oz., both being invaded with the growth; the cervical glands were practically unaffected. Among five cases of lymphadenoma recorded by these writers two had jaundice.

Hyperplastic Lymphatic Splenomegaly.

The relative value of splenectomy and X-ray exposures in disease accompanied by splenomegaly is obviously a matter of practical importance. In spite of the tendency to produce adhesions, and so render subsequent operation more difficult, X-ray treatment would appear to be worth a trial in cases of splenomegaly of doubtful origin, as they may be examples of the condition called by Brill, Baehr, and Rosenthal "splenomegalia lymphatica hyperplastica." They record three cases, none in children; in two, one of which proved fatal, splenectomy was performed, and then it was found that radiotherapy caused complete disappearance of the general lymphatic gland enlargement and reduction of the spleen to its normal size. The condition, which may sometimes pass unrecognized, is characterized by a normal blood-count, general enlargement of the lymphatic glands, and great splenomegaly. The microscopic appearances consist in enormous enlargement of the Malpighian bodies, which are almost entirely composed of endothelial or reticular cells, and of the follicles of the lymphatic glands, which show a similar structure. The condition is not influenced by arsenic, but is rapidly cured by exposures to the X-rays.

(4) TROPICAL SPLENOMEGALY.

Kala-azar.

The infantile form of kala-azar may be seen in children who have come from countries where it is endemic, and the diagnosis depends on the detection of the Leishman-Donovan parasite by splenic puncture. The liver and the spleen are enlarged, but as compared with other conditions are soft to the palpating hand. It occurs in the Mediterranean littoral, Malta, Egypt, and elsewhere, and probably many cases of tropical splenomegaly are due to kala-azar. The *ponos*¹ of the Greek islands

¹ I am indebted to Dr. A. Cawadias of Athens for the following information: *πόνος του Σπένσαι* (the pain of Spetsia) is in the neighbouring island of Hydra known by the name of *τσανακι*, meaning a sort of large plate from the form of the abdomen, and in Cephalonia as *Απλοτινακα*, with the same meaning. These have all been proved to be kala-azar by Gabbi (1910). The disease is relatively common, and the results of treatment by tartar emetic are very good.

Spetsia and Hydra is of this nature. This febrile splenomegaly has been reported in children in the south of France (D'Oelsnitz, Daumas, Liotard, and Puech), and Wyllie has recorded it in a child who came from Malta to England. The treatment is the intravenous injection of tartar emetic and sodium antimonyl tartrate solutions (Rogers). After failing with medical treatment Talbot and Lyon obtained a cure from splenectomy in the first reported cases of infantile kala-azar in America.

(5) MECHANICAL CAUSES.

Enlargement of the spleen due to primary new growth, hydatid and simple cysts, angiomas, and abscess are very rare. Among 57 collected cases of abscess in children 14 only were recognized clinically (La Ferla).

Reference has already been made to the cases with hepatic enlargement or cirrhosis.

BIBLIOGRAPHY.

- BARTLETT, F. H., *Amer. Journ. Dis. Child.*, Chicago, 1922, xxiii, p. 283. BASS, MURRAY H., *Amer. Journ. Med. Sci.*, 1925, clxx, p. 416. BERETERVIDE, E. A., et BIANCHI, A., *Arch. de méd. des enf.*, Paris, 1925, xxviii, p. 144. BOINET, *Arch. gén. de méd.*, Paris, 1903, cxci, p. 362. BRILL, N. E., BAHR, G., and ROSENTHAL, N., *Trans. Assoc. Amer. Phys.*, Philadelphia, 1924, xxxix, p. 371. BRILL, N. E., and MANDLEBAUM, F. S., *Amer. Journ. Med. Sci.*, Philadelphia, 1913, cxlvi, p. 863. BRILL, N. E., and ROSENTHAL, N., *ibid.*, 1923, clxvi, p. 503. CABOT, R. C., *ibid.*, 1913, cxlvi, p. 335. CAMERON, H. C., *Brit. Med. Journ.*, 1917, i, p. 753. CAMPBELL, J. M. H., and WARNER, E. C., *Guy's Hosp. Reports*, 1925, lxxv, p. 433. CARPENTER, G., *Brit. Med. Journ.*, 1903, ii, p. 463. CHANEY, N. C., *Amer. Journ. Med. Sci.*, 1925, clxx, p. 856. CONNER, H. M., *Boston Med. and Surg. Journ.*, 1924, cxc, p. 1. COUTTS, *Brit. Med. Journ.*, 1896, i, p. 1026. COWEN, S. O., *Med. Journ. Austral.*, 1925, ii, p. 279. DE LANGE, C., and SCHIFFERS, *Amer. Journ. Dis. Child.*, 1918, xv, p. 249. D'OELSCHNITZ, DAUMAS, LIOTARD, et PUECH, *Arch. de méd. des enf.*, 1925, xxviii, p. 273. DUKES, W. W., *Arch. Int. Med.*, Chicago, 1912, x, p. 445. FARLEY, D. L., *Bull. Ayer Clin. Lab. Penn. Hosp.*, Philadelphia, 1925, No. 9, p. 45. FRANK, *Berl. klin. Woch.*, 1915, lii, p. 454. FRENCH, H., and TURNER, P., *Proc. Roy. Soc. Med.*, 1914, vii (Clin. Sect.), p. 77. GEE, S., *Brit. Med. Journ.*, 1867, i, p. 435. HALL, A., *Proc. Roy. Soc. Med.*, 1915, viii (Med. Sect.), p. 15. HARVIER et LEBÉE, *Bull. et mém. Soc. méd. des hôp. de Paris*, 1923, 3e sér., xlvii, p. 87. KAZNELSON, *Zeit. f. klin. Med.*, 1917, lxxxvii, p. 133. LA FERLA, L., *Pediatrics*, 1922, xxx, p. 598. LEECH, F., *Ann. Clin. Med.*, 1925, iv, p. 73. MARCHAND, *Deut. Arch. f. klin. Med.*, 1913, cx, p. 359. MARFAN, *Rev. mens. des mal. de l'enf.*, 1903, xxi, p. 211. MARQUARD, E., *Arch. f. Kinderheilk.*, 1923, lxxii, p. 251. MAYO, W. J., *Journ. Amer. Med. Assoc.*, 1924, lxxxiii, p. 815. NÄGELI, "Blutkrankheiten und Blutdiagnostik," 1923. OSMAN, A. A., *Guy's Hosp. Reports*, 1922, lxxi, p. 19. PARISOT, J., et HEULLY, L., *Bull. et mém. Soc. méd. des hôp. de Paris*, 1912, 3e sér., xxxiv, p. 527. POYNTON, F. J., THURSFIELD, H., and PATERSON, D., *Brit. Journ. Child. Dis.*, 1922, xix, p. 143. RICALDO et ALBO, *Bull. et mém. Soc. méd. des hôp. de Paris*, 1924, 3e sér., xlviii, p. 493. RICHARDS, O., and DAY, H. B., *Trans. Soc. Trop. Med. and Hyg.*, 1911-12, v, p. 333. ROGERS, L., "Fevers in the Tropics," 1919, p. 8. STILL, G. F., *Practitioner*, 1904, lxxiii, p. 101. SUTHERLAND, G. A., and WILLIAMSON, B., *Lancet*, 1925, i, p. 323. TALBOT, F. B., and LYON, A. B., *Amer. Journ. Dis. Child.*, 1918, xvi, p. 156. THOMSON, JOHN, "The Clinical Study and Treatment of Sick Children," 1925, p. 425. THURSFIELD, H., "Diseases of Children" (Garrod, Batten, and Thursfield), 1913, pp. 527, 534. TIDY, H. L., *Quart. Journ. Med.*, Oxford, 1923-24, xvii, p. 210. VINCENT, B., *Boston Med. and Surg. Journ.*, 1925, cxcliii, p. 191. WAUGH, H. R., and MACINTOSH, D. S., *Arch. Int. Med.*, 1924, xxxiii, p. 599. WEBER, F. P., "Polycythemia, Erythrocytosis, and Erythremia (Vaquez-Osler Disease)," 1921, p. 71. WEIL, E., *Bull. et mém. Soc. méd. des hôp. de Paris*, 1919, 3e sér., xliii, p. 111. WHITCHER, B. R., *Proc. New York Path. Soc.*, 1925, xxv, p. 25. WILLMORE, J. G., and MACKENZIE DOUGLAS, *Brit. Med. Journ.*, 1925, i, p. 16. WYLLIE, W. G., *Proc. Roy. Soc. Med.*, 1925, xix (Sect. Dis. Child.), p. 5.

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said he intended to confine his remarks to one form of enlargement of the spleen to which Sir Humphry Rolleston had referred, namely, thrombocytopenic purpura hæmorrhagica, in which condition the spleen seemed to play an important part. From the clinical standpoint two important changes consisted in an enlargement of the spleen and a great diminution in the blood-platelets or thrombocytes. From the pathological standpoint these two changes seemed to be associated. The enlargement of the spleen was accompanied by a functional disturbance which took the form of an excessive destruction of blood-platelets, or, possibly, it inhibited their formation. The absence of these platelets led to hæmorrhages, and these constituted the striking feature of the disease. From the therapeutic standpoint, the spleen seemed to be all-important, as no treatment apart from splenectomy had proved of any real value. On the removal of the spleen, the platelets reappeared in large numbers in the blood, and there was a cessation of the severe hæmorrhages.

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The increase in the size of the spleen was not usually great, and was never comparable to that seen in acholuric jaundice or in splenic anæmia. It was more like the enlargement of the spleen met with in typhoid fever; i.e., the spleen was palpable. When the spleen was palpable below the ribs it was probably at least twice or three times the normal size. This splenic enlargement was easily overlooked in the absence of a careful examination. At operations for this disease the spleen was almost always enlarged. In his own two cases in which splenectomy was performed the size was two and a half times the normal in one, and in the other three times the normal. In purpura hæmorrhagica the size of the spleen varied from time to time. He thought the splenic enlargement and the outbreaks of fresh hæmorrhage tended to coincide. When several doctors were examining cases the question of enlargement of the spleen was a difficult one, and opinions varied very much. He had hoped to learn more from Sir Humphry Rolleston on the diagnosis of splenic enlargement, and if everyone was not now fully prepared to diagnose an enlarged spleen, blame for that must be placed on to Sir Humphry's shoulders!

He agreed with what Sir Humphry Rolleston said about slight enlargement of the spleen in babies. During the first year of life these enlargements were not, he thought, of any great importance. But if the spleen could be felt between the ages of 2 and 10 or 12 years, it was safe to assume that the enlargement was pathological.

In the diagnosis of this disease two negative points were of some importance. The first was that there were not any definite changes in the red blood-cells or in the white cells, such as accompanied many primary blood diseases. Clinical examination of the blood showed changes of a secondary anæmia, and the degree of anæmia was directly associated with the amount of blood lost.

The second negative point was that, apart from the anæmia and its results, the patient showed no symptoms of disease; indeed, of this disease one might say: no bleeding—no symptoms—no ill-health. Operation should not be recommended in any case showing constitutional or local disease which might account for the hæmorrhage.

With regard to the diagnosis of the disease, he exhibited a chart (kindly supplied by Dr. Bruce Williamson) of a numerous series of cases in which splenectomy had been performed for purpura hæmorrhagica. Most cases began in childhood.

There were certain alterations in the blood which were of very great value. These were (1) a great diminution in the number of platelets; (2) a prolongation of the normal bleeding time from two or three minutes to ten to twenty minutes or longer; (3) a normal formation of blood-clot, but a failure on the part of the clot to retract and express the blood-serum. These conditions were always present, in varying degree, when the disease was in an active stage. In the intervals which characterized the disease the blood changes might be absent, or at least less striking.

With regard to the forms of hæmorrhage, petechiæ were present in all cases, and large ecchymoses, spontaneous or traumatic, were common to all. The gravity of the disease seemed to reside in the bleeding which occurred from the nose and the uterus especially, less frequently from the bowel or the kidneys. This bleeding might reduce the patient to a condition of profound anæmia, great debility and chronic invalidism.

With regard to the treatment of thrombocytopenic purpura hæmorrhagica in its chronic and recurrent form, medical means had proved most unsatisfactory. As the bleeding usually stopped of itself after a longer or shorter time, many hopeful therapeutists had thought they had succeeded by the use of hæmostatics, but recurrence of the bleeding taught them their error, while if no recurrence ensued they added one more to their delusions. Large blood transfusions seemed to benefit for a time, i.e., as long as the transfused blood was active in the body—a matter of a few days. The only real advance in the treatment of this disease was surgical, namely, removal of the spleen. For the present, however, the diagnosis had better be left in the hands of the physician.

DR. LEONARD G. PARSONS (Birmingham).

In the remarks that I have to make, I propose to follow the suggestion of Sir Humphry Rolleston and to speak of conditions in which there is a considerable degree of enlargement of the spleen. I shall confine myself almost entirely to observations on Banti's disease, acholuric jaundice, and lymphadenoma.

(I) BANTI'S DISEASE.

I must apologize for the use of the term Banti's disease, since not only has the existence of Banti's type of splenomegaly in childhood been denied by many authorities, but also the existence of a specific disorder which can be labelled Banti's disease.

Poynton, Thursfield and Paterson [1] in their survey of the severe blood diseases in childhood, imply that Banti's disease is a specific disorder in adults, but that in childhood such a diagnosis is practically always wrong. Other authorities suggest that if the symptom-complex does occur, it is due to syphilis, tuberculosis, or some other infection, and the suggestion has also been made that some of the cases are examples of acholuric jaundice. If by Banti's disease is meant the whole complex-splenomegaly, anæmia with leucopenia, cirrhosis of the liver, jaundice, hæmorrhages, and gastric symptoms, then the condition is of extreme rarity in childhood. But if it be admitted that this group of symptoms constitutes Banti's disease, I cannot see how the title can be denied to the earlier stages of a splenomegaly, of unknown ætiology, which is combined with an anæmia having no typical blood-picture, except a leucopenia, and in which there is a negative Wassermann reaction, normal fragility, and absence of glandular enlargement. To label these cases splenic anæmia leads to confusion with von Jaksch's anæmia, since there seems no ground for the view that the latter is an infantile form of Banti's disease.

I propose to give some details of three cases of splenomegaly, which I think should be classified as Banti's disease, and which can be regarded as illustrating certain stages in the development of the disease. I am not prepared to admit that the fully developed symptom-complex does not occur in childhood, because the first case seems to fulfil all the necessary criteria.

A girl, aged 11 years, had been in poor health for four years before admission to hospital. During this time she was noted to tire easily, and was treated for anæmia. For six to seven weeks preceding her admission to hospital her abdomen had been swollen.

On admission the abdomen was seen to be swollen, with a large number of enlarged veins on the surface, ascites was present, the spleen was felt two inches below costal margin, the liver one and a half inches below the costal margin.

The blood-picture did not show any characteristic abnormality. The red cell count varied during the six months she was under observation from 3,900,000 on admission to 2,000,000; the white cells from 6,000 on admission to 2,800; rising on one occasion to 7,500. Towards the end of the six months the leucopenia became more marked, and the count was in the neighbourhood of 3,000.

The spleen appeared to vary somewhat in size, the ascites certainly varied, and at times was very marked. There was no jaundice and the Wassermann reaction was negative. Splenectomy was performed in November, 1921. At the operation the spleen was much enlarged and showed adhesions. The liver was enlarged and obviously cirrhotic, the cirrhosis being of a coarse type. The child made a good recovery from the operation, and for the last two years has been earning her living as a factory hand in a box-making factory. She looks well, there are no obvious signs of anæmia, the liver is much reduced in size, being only just palpable, and there is a complete absence of ascites.

The second case is that of a girl, aged 8 years, who was seen to become pale at dinner. The day following, her stools were black, and the day after that there was profuse hæmatemesis. On examination her doctor found that she was very anæmic, had a large spleen, and that there was a little free fluid in the abdomen. A blood-count showed 2,500,000 red cells, 5,000 white cells and there was nothing characteristic in the blood-picture. She

was under my observation for three weeks before splenectomy was performed and during that time her red cell count varied from 5,900 to 6,200.

There was nothing abnormal in the differential count, and the appearances of the red cells were those of secondary anæmia. The spleen was enlarged to within an inch of the umbilicus, and did not appear to vary in size. The slight amount of free fluid in the abdomen increased, and a specimen of the fæces, examined four days before the operation, showed red blood-cells. A slight indirect Van den Bergh reaction was present. Splenectomy was performed, after a preliminary blood transfusion. The child made an uninterrupted recovery. Three days after the operation the red cells were 4,000,000, and the white cells 14,000. Five days before discharge the red cells were 4,800,000, and the white cells 11,250. At the operation the vasa brevia were distended, but the liver appeared perfectly normal, in spite of the hæmatemesis and melæna.

If such a symptomatology as the foregoing can be diagnosed as Banti's disease, I should like to suggest that a leucopenia, although a very important point in the diagnosis of Banti's type of splenomegaly, is not an absolutely essential one. A leucocytosis is stated by some authorities to occur when a secondary infection develops, or after a hæmorrhage. I know that this is not always the case, and some hold the view that leucocytosis never occurs.

A child aged 2½ years was running about in the morning perfectly well, became languid and restless in the afternoon, complained of abdominal pain, and in the late evening vomited about 2½ oz. of blood. On admission to hospital she was seen to be well nourished, but pale. The spleen was considerably enlarged, being about two fingers' breadth below the costal margin. The liver was palpable, with a firm edge, but there were no other abnormal physical signs. The Wassermann reaction was negative. Splenectomy was performed some seven weeks later; during this period her red cell count had varied from just under two million to two and three quarter million, the white cells, which on admission were 7,800, became a week later 9,200, and a fortnight after admission had reached 18,000. After that the number decreased; they were 10,000 one week before operation, and immediately before operation they had fallen to 6,400. There was nothing characteristic about the blood-picture, which showed a fair number of normoblasts. Her abdomen became distended, and apparently contained some free fluid. The fragility of the red cells was normal. In spite of the large white count, amounting at one period to a leucocytosis, the diagnosis of Banti's disease was made. An attempt to assess the liver function, by the bromsulph-phthalein test, was made. This showed a retention of 25 per cent. of the dye after thirty minutes. This figure is one usually found in cases of cirrhosis of the liver, but does not imply grossly impaired liver function, and although the normal amount of dye retained after that period of time is 5 per cent., a normal child will yet, at times, show as much retention as in this case. It is interesting to note that at operation the liver appeared perfectly healthy, as did also the vessels of the splenic pedicle, but the spleen itself showed early capsular perisplenitis.

I would therefore suggest that there is a definite form of splenomegaly in childhood, of unknown ætiology, which is characterized by an anæmia, of the secondary type, but showing no definite blood-picture; characterized also by the absence of certain other signs, namely, a positive Wassermann reaction, glandular enlargement, increased fragility of the red blood-cells. This form should, in the present state of our knowledge, be called Banti's disease.

It is stated that jaundice may occur in Banti's disease, that it does not appear to be dependent upon the liver involvement, and that it is subject to periodic variations. If this be true, the diagnosis from acholuric jaundice may furnish some difficulty. Some evidence in favour of these statements is afforded by the second case which I have quoted, in which an indirect Van den Bergh reaction was obtained, and in which the liver was normal at the time of operation.

(II) ACHOLURIC JAUNDICE.

I have not had experience of vital staining, by brilliant cresyl blue, for reticulation of the red cells, an increase in the number of which is regarded by American writers as an important point in the diagnosis of splenomegaly due to acholuric

jaundice. In the diagnosis of this disease I place the greatest reliance on the occurrence of increased fragility of the red cells, and I think that the best method of testing for this is the one which we now use, and which was elaborated by Dr. Hillier.

Blood is collected from a vein, and placed in a paraffin-coated capsule, from which 20 c.mm. are taken with a hæmoglobinometer pipette, and put into 2 c.c. of the various strengths of saline solution. The tubes are rolled between the fingers to mix the blood and the salt solution, and then centrifugalized. The tube containing the highest percentage of salt, but showing no red sediment, is taken as the standard for complete hæmolysis. The other tubes, showing sediment, are measured against that in the complete hæmolysis tube, in a Leitz colorimeter. The readings give the percentages of the red cells hæmolysed in the various tubes. An important point in diagnosis is not only that hæmolysis starts at a higher percentage of saline than normal, but also that the range over which hæmolysis occurs is greater than normal.

One of my cases showed polycythæmia, and in the so-called "crises of deglobulization," bile appeared in the urine, and the stools became pale.

The most marked degree of anemia, in my experience, was in a congenital, but not familial, case, in which the red cells after a crisis were less than one and a half million (1,380,000). These rose three weeks later to two and three-quarter millions, and splenectomy was then performed. Two months after this operation the red cells numbered almost five millions, and the jaundice had disappeared. The fragility had improved considerably, but was still greater than normal.

At the operation several small red masses were seen at the hilum of the spleen, and it was doubtful whether these were spleniculi or hæmolymp glands. An accessory spleen the size of a walnut was found in the gastro-lienal ligament, and removed.

It would be interesting to know whether these glands or accessory spleens could enlarge sufficiently to reproduce the symptoms of the disease, and if an attempt should be made to remove them. A recent paper by Campbell and Warner [2] contains the statement that there is some evidence that hæmolymp glands or accessory spleens may hypertrophy, but that this does not reach such a degree as to reproduce the original picture.

Indications for Splenectomy.

The treatment of Banti's type of splenomegaly and the splenomegaly of acholuric jaundice by splenectomy is now accepted practice, and the results of such treatment are excellent. I have not had any experience of preliminary treatment of the spleen by X-rays, or radium, in Banti's disease. I feel sure, however, that the operative mortality in both conditions is considerably reduced by a blood transfusion, immediately preceding the operation, and also by postponing operation for a short period if there has been a recent hæmatemesis, or an acholuric crisis.

I do not consider the operation essential in the slighter forms of acholuric jaundice, but the operative mortality is now so small that I think the risk is one that is well worth taking, even in these cases. I cannot bring myself to believe that Moynihan's diets are correct, at any rate in children, viz.: that (1) "no operation for hæmolytic jaundice is complete until the bile passages have been thoroughly explored," and that (2) "the removal of the appendix will be performed in all cases in which the condition of the patient does not prohibit the very slight additional manipulation" [3].

I would suggest that splenectomy be considered the routine treatment for all cases of splenomegaly which show a negative Wassermann reaction, no enlargement of glands, and no characteristic leucocytic picture, but in which there is some degree of anæmia, associated with (1) leucopenia, or (2) increased fragility of the red cells with an indirect Van den Bergh reaction, or (3) hæmatemesis.

It must be admitted that syphilis can produce a picture almost identical with that of Banti's disease, but if such a case showed evidence of cirrhosis of the liver,

or hæmatemesis, and resisted treatment, I do not think that a splenomegaly is necessarily contra-indicated, in fact there is definite evidence to the contrary. I may perhaps be allowed, in this connexion, to refer to a case under the care of my colleague Dr. A. P. Thomson, in which a young adult showed splenomegaly, a leucopenia, and a secondary anæmia, and no glandular enlargement. The Wassermann reaction was positive, but became negative after splenectomy, and the patient recovered, although no antisyphilitic treatment was given. I would also suggest that splenectomy should be resorted to in Banti's disease, even when there are signs of liver involvement, because of the first case I quoted and other similar cases in the literature, for it appears that the liver is able, if the cirrhosis is not too severe, to make a functional recovery. Hæmatemesis does not necessarily mean that the liver will show cirrhosis, and Sir Humphry Rolleston holds that this symptom is due to the rupture into the stomach of enormously distended vasa brevia (noted in my second case).

I realize that if these criteria for splenectomy are accepted literally, on rare occasions a lymphadenomatous spleen will be removed, or even a spleen from a case of aplastic anæmia (anæmia gravis), for in both these conditions splenomegaly, anæmia, and leucopenia may occur. There should, however, be no difficulty in excluding these cases, because the degree of anæmia is so great and striking. The child's skin is so pale as to look almost transparent, contrasting markedly with the rather muddy, or icteric, tinge of Banti's disease, or acholuric jaundice. The appearance is such that I believe anyone who has seen these cases would not think of classifying them in the splenomegalies of Banti's group, or of acholuric jaundice. In lymphadenoma there is, of course, usually enlargement of the external lymph glands, but I have seen at least one case showing this aplastic picture in which there was not any enlargement of the external glands.

(III) LYMPHADENOMA.

Of splenomegaly due to Hodgkin's disease, I would only point out one or two difficulties in diagnosis that have recently presented themselves. I have seen a small group of cases which exhibited the clinical appearance of an aplastic anæmia. In these cases, the pallor has been extreme, of the type to which I have just referred. Two of the cases showed a leucopenia and one a leucocytosis. In one of these cases a few nucleated rod cells were present, but Poynton, Thursfield and Paterson, in the paper to which reference has already been made, state that this may occur in what they call anæmia gravis, a term which they use instead of aplastic anæmia.

One of my cases did not show any external glandular enlargement during the whole of the illness, and another case did not show any until the eleventh week of an illness which lasted fourteen weeks. The latter patient, although a leucopenia was present during the greater part of the illness, showed in the early part of the illness a leucocytosis of 31,000. Shortly after this blood-count was made she developed an abscess under the right side of the jaw, which was duly opened. She had some carious teeth, but the jaw itself appeared normal. An interesting point is that after the operation the spleen became very much smaller until it was only just palpable, but later it enlarged again.

Anæmia gravis is, in my experience, a very rare disease, and to see three cases, such as those discussed, in a short space of time, suggests that the question of lymphadenoma should be considered very carefully before making a diagnosis of anæmia gravis.

The other symptom which characterized two of these cases—and I have known it to occur in other cases of lymphadenoma—was pain in the limbs.

In one case the pain was present in all the limbs, in the other case chiefly in one leg, but also in the arm of the same side. The pain in one case suggested the possibility of an osteomyelitis, although there was no tenderness, but an X-ray showed normal bone. I am aware

that cauda equina pressure symptoms have been described by Parkes Weber [4] and others, but at autopsy there was no evidence of nerve involvement. The pains recalled more than anything the "rheumatic" pains which occur in the early stages of malignant hyper-nephromata, but were rather more severe.

Towards the end of their illness both children complained of pain in the lower part of the abdomen, for which no cause was found post mortem.

In regard to treatment of these children, it is interesting and important to note that X-ray treatment of the spleen definitely made them worse, this being due undoubtedly to the aplastic type of their anæmia.

REFERENCES.

- [1] POYNTON, F. J., THURSFIELD, H., and PATERSON, D., *Brit. Journ. Child. Dis.*, 1922, xix, p. 143.
[2] CAMPBELL, J. M. H., and WARNER, E. C., *Guy's Hospital Reports*, 1925, lxxv, p. 493. [3] MOYNIHAN, Sir B., "The Spleen and some of its Diseases," Bristol, 1921. [4] WEBER, F. P., *Quart. Journ. Med.*, 1923, lxx, p. 1.

Dr. HUGH THURSFIELD

said there was an old story of an oriental monarch who boasted that where his horse had trodden no blade of grass could grow. To-night the members of the Section had been hearing the address of Sir Humphry Rolleston, who, in medical research into any literature he took up, was a modern example of that oriental sultan. It was extraordinarily difficult to speak on any subject which Sir Humphry had tackled as an introducer and to find any portion of such subject that he had not touched upon.

And since listening to Sir Humphry Rolleston, the Members had been hearing a "sultan" from Paddington Green Children's Hospital, and a "sultan" from Birmingham—a fact which made his (Dr. Thursfield's) task even more difficult. With a certain number of the pronouncements of all those "sultans" he cordially disagreed. He disagreed with Sir Humphry in wishing to exclude the first two years of life. Enlargement of the spleen in that period was not only extraordinarily important, but it was not very uncommon.

He wished to attack the subject from the standpoint of enlargement of the spleen at certain definite ages, i.e., definite enlargement, such as no one in the room could possibly miss. At the age of four months and under, enlargement of the spleen was due to one of two main causes: tuberculosis and syphilis. Myelocytic leukaemia was occasionally met with at that age. Certain conditions of septicæmia would also cause enlargements of the spleen under four months of age. If, however, one saw a baby who was obviously very ill with signs which would suit those of tuberculosis, the discovery of an enlarged spleen was, to his mind, clinching evidence of the fact that the child was suffering from tuberculosis. Therefore, in the case of these young babies, it was very important to examine carefully for evidences of enlarged spleen. In regard to syphilis, he did not think he had ever seen a case of syphilitic periostitis in which there was not a definitely enlarged spleen. And, here again, in a child of four months of age, if syphilis was suspected the presence of an enlarged spleen would clinch the diagnosis, whatever the report as to the Wassermann reaction might be.

In the period between 4 months and 3 or 4 years, he thought enlargement of the spleen was comparatively uncommon. One met with it from time to time, but many such instances were not enlargements so much as displacements, due to splaying out of the ribs and flattening of the dome of the diaphragm, thus giving to the spleen an undue prominence.

At about 5 or 6 years of age there was another series of enlargements, and he wished to draw attention to a group of which no mention had yet been made. A child came in fairly ill with a certain degree of anæmia, with a very definitely enlarged spleen, and usually also an enlarged liver. Those cases, in his experience, had always been

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called Banti's disease, but, he thought, wrongly, because by the time one had finished the Wassermann, the corpuscular fragility, and the tuberculin tests, the enlargement of spleen was already beginning to disappear, the liver had become smaller, and the child was getting well. To what that splenic enlargement was due he did not know, but he was convinced that the cause was an infection. One such child he had followed up for many years. The spleen remained palpable—but not enlarged in the sense used by Sir Humphry Rolleston—for two or three years afterwards; it then became impalpable and had remained so. Last time he saw that girl she was aged 17, and had remained in good health. More recently there had been at the hospital two other similar cases, in which the patients had gone out and had remained in good health.

He was leaving big gaps in the subject, but must hasten on. Between 5 and 6 years of age he did not think that syphilis, or tuberculosis, was a common cause. But every now and then one saw a case of definite cirrhosis of the liver and enlargement of the spleen.

From that time onwards, he thought, enlargements of the spleen were uncommon, comparatively, but when they did occur, the diagnosis would usually rest between tuberculosis, syphilis, and lymphadenoma. Syphilis, it was considered, could be excluded when there was a negative Wassermann test, done by a competent pathologist. Tuberculosis he did not regard as a common cause. There was one point about tuberculous enlargement of the spleen between 6 and 12 years which was worth mentioning. As Sir Humphry Rolleston had said it was commonly a tender spleen, and further, nearly all such cases had a polycythæmia, i.e., 8 to 10 million red cells. A further point was that these children did not, as a rule, give subcutaneous tuberculin reactions. If these cases were seen at operation or post mortem, the spleen was the seat not of ordinary tubercle, but of large caseous masses, often the main lesion in the body, the disease having been progressive in the spleen alone. Therefore, if the condition could be diagnosed, he thought removal of these spleens was justified.

Lymphadenoma he regarded as the commonest cause of considerable enlargement of the spleen between 6 and 12 years of age. There were a number of cases in which, for a period of time, it was very difficult to be sure of the diagnosis. When the conclusion was reached that neither the diagnosis of syphilis, tuberculosis, or lymphadenoma, could be sustained, he was strongly opposed to putting the case forthwith into the category of Banti's disease, which he regarded as a diagnostic rubbish-heap. If that name was going to be used, he thought it should be only for such cases as Banti described. Cases of that disease by definition showed a leucopenia.

He thought people had rather left out of sight the importance of acute and sub-acute infections in considering this question of enlargements of the spleen. There was no one of the ordinary acute infectious fevers of children, including measles, chicken-pox, whooping-cough and mumps, in which he had not seen very considerable enlargement of the spleen, i.e., half-way to the iliac crest. In the case of such enlargements the fever might pass and the child convalesce, but it would be some time before the spleen resumed its normal size; that was particularly true of catarrhal jaundice in children. In some of these latter cases the spleen was very large, and it remained palpable after the recovery of the child from the illness.

Lastly, when the spleen had been removed in a case of acholuric jaundice, he could not agree with Sir Humphry Rolleston that the fragility of the blood-corpuscles was not altered. He had at least three cases, which he had followed for many years, and in which removal of the spleen was followed by complete normality in regard to fragility of the corpuscles. There was not much alteration a month or so after the operation, but if examined months, or years, afterwards, the fragility of the corpuscles would be found to have become normal or even abnormal.

Dr. GRAHAM FORBES

said that with regard to spleno-medullary or myelocytic leukaemia—to which but little reference had so far been made that evening with the exception of the case quoted by Dr. Thursfield in a child aged two years—the condition was very rare in childhood. Some years ago he had had the opportunity of collecting a few cases, one of which he had seen at the Hospital for Sick Children, Great Ormond Street.

It was that of a boy, 10 years of age, who had had enlargement of the spleen four months previous to admission. When the boy came in, the spleen was enormously enlarged, reaching down into the pelvic fossa and to the right of the umbilicus. He was in the hospital three months, and when discharged was in much the same condition, except that he had gained over 1 lb. in weight. The spleen felt somewhat harder, but was not reduced in size. The leucocyte count varied from 535,000 to 115,000 per c.mm. in the course of six or seven separate counts and the myelocytes ranged between 26 per cent. and 14 per cent.

Search at the time through some 5,500 post-mortem records of the hospital yielded only one other similar case, and that was in a child aged 3 years and 9 months. It was regarded as a case of *mixed* leukaemia, having 25 per cent. large mononuclears and 14 per cent. myelocytes with a total count of 100,000 to 130,000 leucocytes per c.mm. The child died after an illness of four months. Dr. Hutchison, in his Goulstonian Lectures delivered in 1904, after a considerable search through the literature had been able to collect four cases, one of which had occurred at the London Hospital. That patient was a child aged just under 5 years, with a leucocyte count of $1\frac{1}{2}$ million, and 56 per cent. myelocytes. The other cases quoted by Hutchison were aged 8 and 9 years, and showed counts of from half a million to a million leucocytes, with 67 per cent. myelocytes. He (the speaker) had found records of two other cases: one by Falconer, in Edinburgh, in a child aged 5 years, and the other, reported by Fowler, in Bradford, was that of a child aged 6 years. These, together with the two cases which he had put on record from Great Ormond Street Hospital¹ made a total of eight cases of undoubted spleno-medullary leukaemia in childhood. The rarity of the disease in early life was in striking contrast to its comparative frequency among adults, and to the relatively common blood conditions in children associated with the presence of myelocytes and with or without some enlargement of the spleen. Since then Pisek,² in 1916, had stated that after a careful search of the literature he had collected only nineteen authentic cases of this type of leukaemia in children, seven of which were under two years of age. (Quoted in Abt's "Pediatrics," iv, p. 560, 1924.)

Whatever the exciting cause of true myelocytic leukaemia might be, it would appear to be far less active in childhood than in later life.

In regard to treatment, arsenic, usually advocated, gave little more than temporary relief. The use of deep X-ray therapy, however, in adult cases had led to marked improvement, shown by the reduction in size of the spleen and a fall in the total leucocyte and myelocyte counts, as recently demonstrated at Guy's Hospital by Dr. J. Carter Braine and Dr. L. Watt.

Dr. F. J. POYNTON

said he considered that the profession was now awaiting fresh investigation on the lines of infection; as to whether some still undiscovered organism was at work in these conditions or whether there might not be a peculiar blood reaction to infections—ordinary infections—in some individuals. There was an increase of polymorphonuclear leucocytes in suppuration, there was an increase of mononuclears in glandular fever, and he had wondered whether certain persons might not react in some special

¹ *St. Bart's Hosp. Rep.*, 1906, xlii, pp. 110-112.

² *Arch. Pediatr.*, 1916, xxxiii, p. 938.

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way, so that instead of the usual leucocytes, embryonic cells were formed in response to certain phases of infection. These matters required further elucidation before the law could very well be laid down. Another necessity was a further study of the reticulo-endothelial system.

He was sorry to observe a tendency so strongly towards surgery exhibited on the part of the speakers that evening. In by no means all cases of congenital acholuric jaundice were there fragile corpuscles; he had had several examples in which such fragility had not been found, especially when there were three or four cases occurring in one family; the last of them might show an enlarged spleen but no fragility of corpuscles. He had shown, at a Medical Society of London meeting, a case he had been watching twenty years, in which three skilled observers investigated the blood, and were unable to detect any fragility. With regard to Banti's disease, there had been under his care at Great Ormond Street one boy who had severe hæmatemesis. He was well, except for an enlarged spleen. His blood showed no peculiar characters except a slight leucopenia. Wassermann and other tests were carried out. He had been in hospital a fortnight, when one day as he was lying on a couch, he suddenly sat up, vomited blood, and died. Post mortem it was found that a vein in the œsophagus had ruptured, but there was no cirrhosis of the liver, and no thrombosis could be found in any splenic vein. Nevertheless, he agreed with Dr. Parsons that there was a type of case in children in which the spleen was enlarged and blood was vomited, as was seen in the splenic anæmia of adults. He was not prepared to say that a case of this kind was necessarily one of Banti's disease, or would eventually become such; he could only say that he did not know.

DR. F. PARKES WEBER

made some remarks with reference to the occurrence of leucopenia in enlargements of the spleen. He thought it could be met with in almost any kind of chronic enlargement of the spleen, even in some rare cases of (atypical) leukæmia and could not be used as important evidence of "Banti's disease."

Another point was that there were certain very rare cases of splenomegaly due to atypical leukæmia, in either children or adults, in which there was extreme anæmia, and in which, indeed, death might actually result owing to a kind of aplastic anæmia. In such cases there occurred a more or less complete cessation of the formation of red cells and of polymorphonuclear leucocytes in the bone-marrow, and death was the result of this aplastic condition. In some such cases transfusion of blood might be tried at an early stage.

With regard to congenital and familial chronic acholuric jaundice or hæmolytic jaundice, in exceptional cases there might be an absence of that characteristic sign, the diminished resistance of the erythrocytes (as tested by graduated hypertonic sodium chloride solutions). Dr. Poynton had just referred to a striking example in illustration, and on the continent Gänsslen¹ had traced all the relatives of typical cases of congenital hæmolytic jaundice, and had found that some members of the families exhibited mild, incomplete and atypical forms of the disease. In some the spleen was enlarged with slight jaundice; in others there was no obvious jaundice, but slight anæmia; in a very few no increased fragility of red cells was found. Therefore, could anyone seriously advocate splenectomy in every case of congenital familial hæmolytic jaundice? Such an idea would be impossible to carry out, and one must remember that the prognosis without splenectomy was good in many cases, both in regard to average longevity and in regard to leading a useful, if not a very strenuous, life.

¹ Gänsslen, Zipperlen and Schütz, *Deut. Arch. f. klin. Med.*, Leipzig, 1925, cxlvi, pp. 1-46.

Section for the Study of Disease in Children.

President—Mr. PHILIP TURNER, M.S.

Measles Complicated by Gangrene of the Legs.

By D. J. HISHON, M.B. (introduced by J. D. ROLLESTON, M.D.).

A MALE infant, aged 16 months, was admitted to hospital on October 23, 1925, suffering from measles, on the second day of the rash, with signs of commencing broncho-pneumonia; the general condition was poor.

On October 25 the rash had faded and the signs of broncho-pneumonia were more marked. The heart sounds were rapid and weak but regular. There was no evidence of endocarditis. During the latter stage of the illness the heart sounds were practically inaudible owing to rapid respirations and the presence of numerous adventitious sounds in the left lung. From October 28 to November 3 the patient became progressively weaker. The colour was poor, dyspnoea extreme and the temperature between 99° F. and 103° F. The extremities, especially the legs and feet, were cold and blue. The cyanosis at intervals passed off leaving the parts cold and pale.

On November 3 distinct patches of discoloration varying in size from that of a shilling to that of a half-crown were observed on the dorsal surfaces of both feet. The soles were cold, blue and anæsthetic; the toes were bent and retracted, and the patient was apparently unable to move his lower limbs. The femoral and popliteal pulses could not be felt, but no alteration was detected in the radial pulse. The temperature, which had ranged between 99° F. and 103° F., became subnormal and remained so until the end. On November 4 the whole of the dorsal surface of the right foot was discoloured and the dorsal surface of the left foot to a lesser degree. Patches of discoloration were observed on the lower two-thirds of the right leg and the lower third of the left leg. On November 5 these patches had coalesced and a line of demarcation was obvious on both legs, being more defined on the right leg. The discoloration on the left leg seemed less vivid at times, parts of the skin appearing only slightly cyanotic. The systolic blood-pressure taken in the brachial artery had fallen to 40 mm. Hg. On November 7 the patient was obviously much weaker, and death took place on November 8.

Necropsy.—Both popliteal and superficial femoral arteries contained ante-mortem blood-clot throughout their entire course. The left kidney showed a pale infarct on its vertebral border below the hilus. The liver and spleen were engorged. A large vegetation, about the size of a pea, occupied the upper surface of the anterior aortic valve.

REMARKS BY DR. ROLLESTON.

When one compares the proceedings of this Section with the proceedings of other pædiatric societies, one cannot help noticing that acute infections occupy a very small part of our proceedings. That is to be accounted for in more than one way. First, it is due to the fact that acute infectious diseases in this country—London in particular—are cared for in isolation hospitals, whereas abroad, and particularly in Paris, Berlin and other continental cities, there are pavilions or blocks

for infectious diseases in the grounds of the children's hospitals. Another reason is that perhaps not enough enthusiasm is shown by the medical officers of isolation hospitals in bringing forward interesting cases. It is for that reason I have asked my colleague, Dr. Hishon, to bring forward this very interesting and rare case of gangrene of the leg following measles. Gangrene of a limb following an acute infection is very rare, so rare that it does not figure in most of the textbooks. On the other hand, it is interesting that it is one of the earliest complications of an acute infectious disease to be described in the history of medicine. Hippocrates, in the Third Book of the Epidemics (Sect. iii), describes loss of limbs as a complication of fevers. And again, in a description of the Plague of Athens, Thucydides (Bk. ii, c. 49) relates how many recovered after losing their hands, their feet and their genitals. Many attempts have been made to identify this mysterious Plague of Athens with various acute infections, but probably it will never be identified. Estlander, who thinks it was typhus, refers to the occurrence of gangrene in typhus in the Middle Ages, and in the sixteenth, seventeenth, and nineteenth centuries.

So far as I know, only two previous cases of gangrene of a limb following an acute infection have been shown at this Section. The first was a case which I showed over fifteen years ago, following diphtheria. A boy aged 13 years had a severe attack of diphtheria, and on the thirtieth day developed gangrene of the left foot. It was not until six weeks later that his condition allowed of operation, and he was then transferred to Charing Cross Hospital, where amputation at the knee-joint was performed by Mr. Clogg, and he made a good recovery. Six years later, Dr. Gunson reported before the Section another case of gangrene. There was a similar history of diphtheria, with cardiac changes. The gangrene developed in the third week, and amputation about the middle of the knee was performed about six weeks afterwards. Again Mr. Clogg operated, and a perfect recovery ensued. I collected the records of eleven cases in 1910, and since that date a number of others have been reported after diphtheria. In 1918 Robbins collected records of twenty-five cases, which he published in the *Medical Record*. Generally speaking, gangrene of the leg is commoner after typhoid and typhus than after any other acute infection. I sent a reprint of my paper on gangrene to Professor Osler, who said the subject was of great interest to him, and that he had had one or two cases after typhoid. I now show a chart of all the cases of gangrene of the limbs following measles, besides the present case.

As to the pathogenesis, in this case it is embolic, just as in the cases following diphtheria which were shown before the Section. No doubt some of them are due to autochthonous thrombosis. Lutz made post-mortem examinations on twenty-two cases of measles, and found eight cases in which there was more or less thrombosis of the pulmonary arteries. Thus, though thrombosis is comparatively common in measles, one seldom gets occlusion of the vessels of the limbs. In conclusion, I would allude to the rarity of gangrene generally in measles. In text-books, emphasis is laid on cancrum oris as important in measles, but during twenty-five years' experience in fever hospitals I have only seen one or two cases, and only one of noma pudendi. This is probably due to the improved conditions of hygiene and nursing.

REFERENCES.

- BARANGER, *Bull. Soc. de Péd. de Paris*, 1923, xxi, p. 384. BARLOW, *Lancet*, 1887, i, p. 731. BARRAUD, *Deutsche Zeitschr. f. Chir.*, 1904, lxxiv, p. 237. CAPACCINI, *Raccoglitori medico*, quoted by Barraud, *loc. cit.* GALOP, *Arch. de méd. des enf.*, 1914, xvii, p. 42. GUNSON, *Proceedings*, 1916, ix (Sect. Study Dis. Child.), p. 56; *Brit. Journ. Child. Dis.*, 1916, xiii, p. 137. HALES, *Philadelphia Med. and Surg. Reporter*, quoted by Barraud, *loc. cit.* KOLB, quoted by Barraud, *loc. cit.* LAUBE, in SCHMUCKER, *Vermischte chirurgische Schriften*, 1782, iii, p. 96. LUTZ, *Berl. klin. Woch.*, 1913, i, p. 1566. MUNK, *Comp. rend. XII Congrès Internat. de Méd. (Moscow)*, 1899, v, p. 611. PAUL, *London Med. Gaz.*, 1831-2, ix, p. 4. ROBBINS, *Med. Record*, 1918, xciv, p. 620. ROLLESTON, *Brit. Journ. Child. Dis.*, 1910, vii, p. 529. THORP, *Lancet*, 1921, ii, p. 754. ZUPFINGER, *Wien. klin. Woch.*, 1899, xii, p. 335.

GANGRENE OF THE LIMBS FOLLOWING MEASLES.

Date	Author	Age yrs. mths.	Sex	Limb affected	Operation	Remarks	Result
1782	Laube	13 —	M	Left foot and leg	Amputation of femur	—	Recovery
1831	Paul	21 —	M	Leg	Amputation of femur	—	Recovery
1870	Kolb	9 —	M	Both legs	—	Post-mortem :— thrombosis abdominal aorta	Death
1871	Hale	22 —	F	Foot	Amputation of femur	Pregnancy, thrombosis, popliteal artery, heart normal	?
1887	Barlow	Child	?	—	—	Symmetrical gangrene	?
1899	Munk	2 11	M	Left hand	Amputation of fingers of left hand	Broncho-pneumonia	Recovery
1899	Zuppingen	5 —	F	Right foot and left leg	Pirogoff amputation left foot, removal of first metatarsal and internal cuneiform	Multiple cutaneous gangrene	Recovery
1899	Capaccini	2 —	F	Right leg	Operation refused	Right foot sloughed off spontaneously	Recovery
1914	Galop	1 7	F	Right foot and leg	Amputation	Broncho-pneumonia	Death
1921	Thorpe	4 6	F	Left leg and right hallux	—	" "	"
1923	Baranger	— 11	M	Left leg	—	" "	"
1926	Hishon	1 4	M	Both legs	—	" "	"

Discussion.—Dr. E. W. GOODALL said he agreed with Dr. Rolleston as to the rarity of these cases. He did not consider that they were due to any specific poison, because they had occurred in most of the acute specific diseases. He had never himself met with a case of such extensive gangrene as that now related by Dr. Rolleston. He had seen slight gangrene of the tips of the fingers in a severe case of scarlet fever, and also, in another case of this disease, little patches of gangrene of the skin on different parts of the body and limbs. And that was all, in a very extensive experience of fever cases. Through the kindness of Dr. Pearson, of the Fever Hospital, Leeds, he showed a water-colour drawing of a symmetrical case of gangrene of both legs, which occurred in a case of scarlet fever nearly thirty years ago. Dr. Pearson published the case (without the drawing he (Dr. Goodall) was now showing) in *The Lancet*, 1897.¹

Dr. Rolleston said that Professor Osler had stated that he had not met with a case of gangrene after scarlet fever, but on looking up Dr. Pearson's account of his case, he had found a reference of Professor Osler's to cases of gangrene of the limbs in scarlet fever. In nearly all the cases of which Dr. Rolleston had collected the notes, the lower limbs were affected, and he (Dr. Goodall) would like to hear from someone present why the lower should be affected, if the cause was embolic, rather than the upper limbs. Also, it was curious why it should so often be symmetrical.

Mr. PHILIP TURNER (President) said he remembered one of these cases, he believed it was the one Dr. Rolleston had shown fifteen years ago. He presumed that in the present case

¹ *Lancet*, 1897, ii, p. 84

the gangrene was of the moist variety, as in the photograph it seemed swollen rather than shrivelled. [Dr. ROLLESTON: It was dry]. He (Mr. Turner) thought that in those cases the cause was probably an embolus, and he did not regard the fact that in almost all cases it was in the lower extremity as against that idea. He considered that in the upper extremity it would be possible for there to be a considerable block in an artery, and, owing to the better anastomosis and better circulation, for no gangrene to occur; whereas, in the lower extremity, the circulation being carried on under greater difficulties and the anastomosis being less free, an embolus there would be more likely to cause gangrene.

A Case of Congenital Stenosis of the *Œsophagus*.

By C. C. BEATTY, M.C., M.B.

MARY S., aged 3 years, first child, full-time normal labour. Partially breast-fed for twelve months with addition of cow's milk and water for the first six months, then Neave's food.

On being weaned at twelve months she began to vomit, and from that time she has continued to vomit all solid food. The vomiting occurs immediately after a few mouthfuls have been taken, and is apparently unaccompanied by nausea, as she will immediately try again. There are periods when even liquids are vomited. She was very constipated, but was otherwise in good health.

When first seen at the Royal Northern Hospital a year ago she was small and thin, weighing only 18½ lb. Physical examination was negative except for a systolic murmur at the base. She was admitted for observation, and in the ward the mother's account was corroborated.

X-ray examination showed a marked narrowing of the *œsophagus* at the level of the junction of the middle and lower thirds. *Œsophagoscopy* was carried out by Mr. Mant, and this showed a very small opening in the narrowed part, with slight puckering of the mucous membrane at the margins. Bougies were passed up to a diameter of one-third of an inch. The temperature rose to 100° F. on the following day, and three days later she was sent home with chicken-pox. Shortly afterwards she developed whooping-cough and was not seen again until July, 1925. Her mother stated that after the dilatation there had been no improvement in swallowing, and her condition remains the same.

The opinion of the meeting is sought as to the advisability of making further attempts to dilate the *œsophagus*.

Discussion.—Dr. DONALD PATERSON said that he regarded this as rather a case of *œsophagectasia* or cardio-spasm. The reasons for his opinion were, first, that if it had been an organic stricture, probably the child would have vomited before it was a year old; secondly, that she was very well nourished for a case of organic stenosis of the *œsophagus*. Vomiting was intermittent, i.e., she could keep down a certain amount of solid food, according to the statement of the father. A third reason, for the case being one of *œsophagectasia*, was that X-rays showed the stricture apparently at different levels. A number of cases of cardio-spasm had been shown at the Section, and they had not always been at the cardiac end of the stomach, sometimes they were at the junction of the lower and middle thirds. In one case of the kind, in which the stomach was opened, the surgeon passed his finger up the cardiac end of the stomach, and found no stenosis at all, yet when viewed by X-rays after giving a bismuth meal, the impression of stenosis of organic nature was given. Dr. John Thomson had once told him of a doctor who had periods of vomiting at intervals over a number of years; that this doctor knew when the spasms were imminent and discontinued his practice for a week or two; he then enjoyed a long span of immunity. In his experience of five cases, the only case which came to a post-mortem was the one which was operated on. If left alone the patients seemed to get on as well as did the doctor of whom he had spoken.

Dr. F. PARKES WEBER asked whether doses of belladonna had been tried in this case; if not, he thought it was worth trying, though the absence of a beneficial effect would not settle the diagnosis. Surely the diagnosis could be made between congenital stricture and "cardio-

spasm" or so-called achalasia. In the typical cases of achalasia the obstruction was at the cardia; it was not there in the present case. The case might be one of congenital stenosis, with just sufficient room for food to pass through the constricted part of the œsophagus.

Dr. EDMUND CAUTLEY said he thought it more probable that this was a case of stricture of moderate degree, definitely extending a good way down and seeming to involve half to one-third of the œsophagus. That vomiting did not occur earlier could be accounted for by the child having been fed on liquid diet. The fact that she could now swallow bread and butter did not count for very much, as that food was converted into pap before it was swallowed. He regarded it as congenital atresia or stenosis, in which the upper part of the œsophagus, instead of ending as these cases usually did in an opening into the trachea, was continued by a pervious fibrous cord into the lower part. The question of diagnosis was very important as the treatment depended on that. If one was dealing with a congenital atresia and practically a fibrous cord joining the two ends of the œsophagus, it was dangerous to try dilatation beyond the size of a No. 12 catheter.

Dr. J. K. BARTON said that some years ago he saw a young lady aged 18, who came with a history of extreme difficulty and slowness of swallowing. Under X-ray examination there was the same appearance as in the present case. She was very healthy, and could play tennis and other games, and was intending to go back to South Africa. The view taken was that it was a functional condition. This was not impossible in the present case, as the child was thriving. If it was proposed to operate, he would suggest gastrotomy being done, as in the case of "Beaumont," with a hole in his stomach, quoted in old books on physiology. From inspection of the skiagram, he would have thought the condition was organic, and he would ask the men up in developmental anatomy if they could give an explanation of the atresia, when there was no history of traumatism or disease that otherwise might have brought about the obstruction. He agreed with Dr. Parkes Weber that this was too long and narrow a passage for cardio-spasm.

Mr. PHILIP TURNER (President) said one ought to examine the patient first, and then look at the skiagram. In the next room he happened to see the X-ray pictures first, and concluded from them that here one was dealing with organic obstruction. On seeing the patient, he was surprised to note how well the child looked. Though thin, she was not badly nourished, and she seemed fairly strong. The father said that sometimes she swallowed bread and butter and bread and milk, apparently without much trouble. After seeing the patient and hearing that history, he (the President) thought it probable that it was some spasmodic condition. With regard to further attempts at dilatation, he considered it was best to keep the child under observation, not doing anything at all for the present. He asked whether there had been any improvement in the child during the last twelve months, as to weight, &c.

Dr. BEATTY (in reply) said he did not regard the criticisms made by Dr. Paterson as very convincing. The child was anesthetized for the œsophagoscopy, but the narrowing did not then disappear. Dr. Paterson had also said the fact that the child did not commence to vomit until twelve months old was against the idea of the stricture being organic; but in the literature the most striking thing was that in practically every case, while the child was taking the breast or milk, there was little or no vomiting, and that the symptoms became noticeable when solid food was taken. Belladonna was tried for only a short while, about a fortnight, and no improvement took place during that time. In answer to the President, the only improvement about which he could be definite was the ability of the child, during the last fortnight, to take and keep down bread and butter. The father's story told to one of the Members differed from that given to him. The weight of the child a year ago was 18½ lb., and it remained at about that level now.

Specimens from a Case of Banti's Disease.

Shown by DONALD PATERSON, M.B.

THE specimens are from a male, aged 4 years, admitted to the Hospital for Sick Children, Great Ormond Street, under Dr. F. J. Poynton, on January 12, 1922, and died February 25, 1922. The complaint was swelling of the abdomen, from which he had suffered for two years, and with hæmatemesis six months before admission. On admission, the spleen was noted three fingers' breadth below the costal margin and the liver two fingers' breadth below. These organs were not

tender on palpation. There was slight enlargement of the cervical and axillary glands. The blood-count was the following: red blood-cells, 2,750,000 per c.mm.; white blood-cells, 2,400 per c.mm.; hæmoglobin 30 per cent.; colour index 0.5; polymorphonuclears 70 per cent., lymphocytes 24 per cent. Fragility of the red cells normal. Blood Wassermann normal. Tuberculin fixation test weakly positive, von Pirquet test negative. During six weeks in hospital the patient was afebrile, then there was a sudden large hæmatemesis, with death. The specimens showed well marked varices at the lower end of the œsophagus. It could be seen at post-mortem that the blood had escaped from one of them. The varices were large and firm like hæmorrhoids. The spleen was large and firm, and microscopic section showed much fibrosis present. The liver was large and pale but did not show cirrhosis microscopically. The diagnosis is an early case of Banti's disease.

Case of Congenital Heart Disease.

By H. C. CAMERON, M.D. (shown by Dr. SIBYL R. EASTWOOD).

M. H., AGED 5½ years.

Family History: Nil.

History and Present Condition.—Has had measles and broncho-pneumonia, attacks of epistaxis every three months for the last two years, attacks becoming more frequent. Heart enlarged downwards to left, and also to right of sternum. Systolic thrill in pulmonary area. Thrill conducted up to large vessels of neck. Loud systolic bruit, loudest over pulmonary area and conducted upwards and to left; reduplication of second sound over præcordium. Water-hammer pulse. No aortic regurgitant murmur.

REMARKS BY DR. SIBYL R. EASTWOOD.

The heart is enlarged to the left, and very slightly to the right. There have been no symptoms indicating a severe condition of congenital heart disease. The child has never been known to become blue on exertion, and this history given by the mother has been corroborated during the short time the child has been in the ward. It was intended that the case should be designated "congenital heart disease, a case for diagnosis," in order that we might have the opinion of Members as to the lesion. The thrill and murmur are compatible with some degree of pulmonary stenosis, but in view of the child's history and the absence of any marked right-sided cardiac enlargement, I believe it to be a case of patent ductus arteriosus.

Dr. G. A. SUTHERLAND said he was inclined to agree this was a case of patent ductus arteriosus. He thought there was a double murmur at the base—an extremely loud murmur, such as was rarely met with except in connexion with a patent ductus arteriosus. There was a definite hypertrophy of the left side of the heart, such as was often present in that condition. He could not make out any definite change on the right side, therefore he did not think it necessary to bring in a suggestion of pulmonary stenosis. Water-hammer pulse was mentioned in the notes, but all he could find was a small weak pulse. A water-hammer pulse required a considerable volume of blood, otherwise there could not be the collapse afterwards. It had been suggested by some that the thrill was too marked to be associated with a patent ductus arteriosus; but the point about thrills generally was that the same factors which caused loudness of murmur would also cause a thrill.

Pseudo-hypertrophic Muscular Dystrophy.

By H. C. CAMERON, M.D. (shown by Dr. SIBYL R. EASTWOOD).

H. M., AGED 9 years.

Family History: Nil.

History and Present Condition.—Condition commenced at age of four, with weakness in back. Progressively getting weaker.

Mr. B. WHITCHURCH HOWELL said that he had at present under his charge four cases of pseudo-hypertrophic muscular dystrophy which were being treated by the same masseuse. They were of totally different origin, with no family history whatsoever. After six or twelve months' treatment, though in these cases the prognosis was usually very doubtful and unsatisfactory, the condition of these four patients was distinctly improved, and in rising from the ground none of them now climbed up their own thighs. He asked whether this improvement was attributable to the fact that they had been treated on the same lines by the same masseuse, or whether the type of disease was now less severe than in former days.

Case of Congenital Ichthyosis and Cyclical Vomiting.

By H. C. CAMERON, M.D. (shown by
Dr. SIBYL R. EASTWOOD).

I. S., AGED 9½ years; third child.

Family History and Present Condition.—Mother suffered from vomiting periodically up to age of puberty. No migraine. Two other children perfectly healthy, no vomiting or ichthyosis.

History and Present Condition.—This child has suffered from ichthyosis since birth. There is periodic vomiting every three months; this has persisted for the last four and a half years.

REMARKS BY DR. SIBYL R. EASTWOOD.

This case is shown mainly because of the interest of the association of the two conditions. I have not had a large personal experience of either cyclical vomiting or ichthyosis, but in a series of cases of the former, seen by Dr. Osman, 83 per cent. of them had a preceding family history of migraine or cyclical vomiting, or both, in the parents or relatives; in 50 per cent. it was the mother who had suffered from one or other condition. Of cases which suffer from cyclical vomiting in childhood, about 50 per cent. develop migraine in adult life and about 50 per cent. appear to recover completely. There is an impression that cyclical vomiting is more common in ichthyosis than in the normal population; in 5 per cent. or 6 per cent. of cases of cyclical vomiting there was ichthyosis. I do not know whether there is a causal association, and it would be interesting if Members meeting with a combination of the two states would report it.

Case of Obesity ? Pituitary in Origin.

By T. GRAINGER STEWART M.D. (shown by
Dr. MACDONALD CRITCHLEY).

BOY, aged 13 years, admitted for headaches and adiposity. Height 5 ft. 10 in.; weight 17 st. 3 lb. Feminine distribution of fat. Sexual characteristics infantile. No ocular disturbance.

Discussion.—Dr. MACDONALD CRITCHLEY said he wished to apologize for the diagnosis he made. Cases of true Fröhlich's syndrome showed bony under-development, but this case showed skeletal overgrowth. It was most probable that the case belonged to some type of dyspituitarism, resembling the cases described by Neurath and Cushing. There had not yet been the opportunity of making all the investigation that was desired as the patient had been under observation three days only. Skiagrams of the skull showed that the sella turcica was small. The blood-pressure was 110. Resting blood-sugar = 0.102 per cent.

Dr. F. PARKES WEBER said that, owing to the great size of this boy at 13 years, his general appearance and the absence of certain other signs typical of Fröhlich's syndrome, he suggested it was a case of primary "hypogonadism," and that the large size and the fatness

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were due to absence of development of the sexual organs early in life. A man castrated after puberty would not develop overgrowth of the skeleton like this, though he might become fat.¹

Dr. E. STOLKIND suggested that in this case there might be both disturbance of the pituitary gland and the disturbance known as hypogonadism.

Mr. PHILIP TURNER (President) said the only case of the kind he had seen was that of a girl aged 13 years who weighed 14 stone. She came to hospital because of very acute appendicitis, needing immediate operation, and it was remarkable to note how deeply one had to incise before coming to the muscular abdominal wall. The patient made a good recovery, and mentally and in every other way she appeared to be well. He believed the sexual organs were normal.

Dr. MACDONALD CRITCHLEY (in reply) said that it was thought to be a case of functional disorder of the pituitary gland, with secondary involvement of other endocrine glands. There was nothing in the form of a gross tumour or cyst in the pituitary region. One could not place much reliance on the fact that the skiagram showed the sella turcica to be small. Blood-sugar curves, he believed, were often important. The boy had undergone no treatment, at least, not for the past few years. His (the speaker's) experience of pituitary gland administration in pituitary obesity had been disappointing.

¹ On the differential diagnosis between primary hypogonadism in children and Fröhlich's pituitary syndrome with *secondary* hypogonadism (dystrophia adiposo-genitalis), see M. S. Reuben and G. R. Manning, "Congenital Hypogonadism," *Archives of Pediatrics*, New York, 1924, xli, p. 489.

Section for the Study of Disease in Children.¹

President—Mr. PHILIP TURNER, M.S.

Case of Auricular Fibrillation.

By G. A. SUTHERLAND, M.D.

W. H., AGED 14 years. Patient has been under observation since 1918 suffering from heart disease of rheumatic origin. Very great cardiac enlargement associated with adherent pericardium and mitral regurgitation. No recent rheumatism. Subject to recurrent attacks of bronchitis.

Three weeks before admission on November 24 the patient was seized with bronchitis and great difficulty in breathing. This continued, and on admission she was still very breathless, with œdema of the extremities and some ascites. The heart was beating very irregularly at a rate of 120-140 per minute. Great benefit from digitalis treatment. Auricular fibrillation has persisted.

I wish to refer to the subject of therapeutics. This patient and the two others shown suffered from great cardiac dilatation and hypertrophy, the result of valvular disease or adherent pericardium. They were able to endure for some years without any symptoms of cardiac distress, although unable to lead lives of full activity. A time came in all three when the heart failed, that is to say it failed to carry on the circulation successfully, and dyspnoea, œdema, &c., developed. There was no real change in the heart itself as regards muscle or valves, but there was a great increase in the ventricular rate. In the one case the ventricular action was irregular, the result of auricular fibrillation; in the other two it was quite regular. There was, therefore, a disturbance of the normal heart rhythm, and the ventricle was contracting so rapidly that it had lost its full contractile power. In all these cases, under the use of digitalis, the ventricular rate was slowed, and when the rate fell to normal the ventricle recovered its former contractile power and all signs and symptoms of cardiac distress rapidly passed off. In the case of children I have found that this action is obtained whether the ventricles are beating regularly or irregularly, but only when the trouble is chronic rheumatic heart disease. Most authorities state that digitalis acts on the ventricles directly and increases the contractile force, but of this there is no clinical evidence—merely a slowing of the ventricular rate through stimulation of the vagus.

Discussion.—Dr. ABRAHAMS said that cases were occasionally seen in which, contrary to all our clinical experience, one was bound to admit what could be only a muscular effect following the administration of digitalis. Since he had heard Dr. Sutherland's teaching on this matter, his own experience had led him to agree with that of Dr. Sutherland. Yet there were cases in which benefit could only have occurred through the digitalis producing a direct action on the cardiac muscle.

Dr. G. A. SUTHERLAND (in reply) said that he agreed with Dr. Abrahams that there were certain cases which gave the appearance of direct benefit to the heart muscle following digitalis administration. Where the heart's action was rapid, digitalis was given for a definite purpose, and that purpose was usually achieved by it, whereas in the kind of case Dr. Abrahams mentioned it was not given very hopefully, and it was difficult to be sure as to exactly how the digitalis had acted.

¹ Clinical Meeting, held at Paddington Green Children's Hospital, February 26, 1926.

44 Sutherland: *Congenital Cystic Kidneys*; Miller: *Lamblia Enteritis*

Case of Congenital Cystic Kidneys and Arterio-sclerosis.

By G. A. SUTHERLAND, M.D.

E. L., AGED 12 years. Seen first in 1920. Complaints were wasting, thirst, polyuria, and frequency of micturition. The urine was of s. g. 1008, averaged in amount 40 oz. per diem, and a trace of albumin was usually present. No local lesion was detected in the urinary passages. The apex beat was strong and the left ventricle evidently hypertrophied. The radial and brachial arteries were hard and thickened and the pulse tension high. Sphygmomanometer reading 180/90. Later a mass was felt on the left lumbar region like an enlarged kidney. There were attacks of acute abdominal pain with vomiting, and a large fluctuating swelling appeared in the right lumbar region (? hydronephrosis). This swelling gradually disappeared. The patient shows delayed development (infantilism), but enjoys fairly good health.

Discussion.—Dr. REGINALD MILLER said that some years ago he made one of the first collections of cases of renal infantilism, and it became clear that one could expect renal infantilism to occur in certain cases of congenital cystic kidney. Up to that time such cases had not been described. The diagnosis in this present case seemed to be well supported by evidence, but the child was fairly old for the condition. In most of the cases he collected, the children were dead before their twelfth year. He would not like to say that this child's kidneys were not granular. Most patients with cystic disease of the kidney died of uremia. He wondered why this child had survived so long, because the non-cystic part of the kidneys was not originally diseased; he would hesitate to say that such disease was not now progressing during the course of the child's life.

Mr. PHILIP TURNER (President) considered that on the left side a considerable enlargement was to be felt, and said that that was compatible with a single cyst bulging forward; it seemed more like that than an enlargement of the whole kidney. On the other side there had probably been a hydronephrosis, which had gradually disappeared, and not a cystic enlargement. He did not know what explanation could be given of a hydronephrosis on one side and a cystic enlargement on the other.

Dr. E. A. COCKAYNE agreed with the President that this did not feel like an ordinary congenital cystic kidney. Such cases were mostly bilateral. He regarded this case as one of ordinary renal infantilism, with one or more large retention cysts in the left kidney, secondary only to the kidney disease.

Dr. G. A. SUTHERLAND (in reply) said that it had not occurred to him that the child was suffering from granular kidney. He assumed that there was only a small amount of renal tissue functioning, and that this explained the polyuria and the low specific gravity of the urine. Possibly, however, the fibrosis which affected the arteries had also implicated the remaining kidney tissue. From the beginning there was a definite mass in the lumbar region. While in hospital the patient had an attack of acute pain in the right side of the abdomen, and there was a large cystic swelling which he took to be hydronephrosis. That gradually subsided, and then one could make out a mass in the right renal region. It was suggested that some of the cysts had become enlarged and were pressing on the ureter. It might be a polycystic kidney, but he did not feel certain about it. The child, certainly from her seventh year, probably from birth, had suffered from renal symptoms.

Group of Cases of *Lamblia Enteritis*.

By REGINALD MILLER, M.D.

(I) R. H., AGED 14½ years (showing gradual subsidence of symptoms without permanent harm). *Lamblia enteritis* since 3 years old; fat in stool about 10 per cent. only. At 9 years was 3 in. below normal height. Diarrhoea lately ceasing to trouble, and growth satisfactory. Has nearly caught up normal height and weight. Has never been toxic, but wiry, although thin.

(II) A. S., aged 2 years. Shows the severer effect of *Lambli*a enteritis usual in youngest subjects. Onset of diarrhoea at 12 months; fat in stool 23 per cent. and 18 per cent. Weight now 23 lb.

(III) O. K., aged 11 years. Diarrhoea for some years; this has affected growth. Patient is of same height as her sister aged 9 years. There are bilateral lymph-angiomatous swellings over parotid regions.

Discussion.—Dr. T. PEARSE WILLIAMS said the theory of *Lambli*a infection had been rejected by protozoologists, as they said the *Lambli*a was not an organism which would produce the symptoms caused by a resident in the intestine. Many cases were encountered in the war, and they all showed the same symptom, namely, diarrhoea, the motions containing undigested food. The *Lambli*a was found high up in the small intestine. He had discovered that *Lambli*a was not an uncommon infection of children in this country, but these were different from the coeliac cases. He asked whether these coeliac children, when taking normal diet, showed any aversion to fat after having been kept on a fat-free diet. Also, were they liable to suffer from acetonæmia?

Dr. REGINALD MILLER (in reply) acknowledged the kindness of Dr. Pearse Williams in investigating these cases of lambliasis. The condition was a very common cause of chronic diarrhoea, and it was remarkable that it was not more recognized. During the last three years there had been between thirty and forty cases at the hospital. Clifford Dobell said that 18 to 27 per cent. of English people carried *Lambli*a. In the hospital it occurred in 5·8 per cent. of consecutive cases; the youngest was an infant three months old. There was no question that in children the *Lambli*a produced symptoms, and some of the children had definitely lost weight. In coeliac disease it was very difficult to ascertain a change in regard to taste for fat. In the active stages of the disease the children had no fancy for food, and some had a real horror of fat. On the other hand, some liked fat; one patient would eat $\frac{1}{2}$ lb. of butter with relish whenever he could purloin it.

Case of Partial Atlanto-axial Dislocation.

Shown by F. G. MUNDELL, M.B. (for D. C. L. FITZWILLIAMS, C.M.G., F.R.C.S.).

THIS patient had an accident nine days ago, and first came up to hospital two days later, complaining of pain in the neck. There were no other symptoms. It was then thought to be a sprain of the neck muscles; some evaporating lotion was given and the boy was sent home. Four days later he returned holding his head with his hands and seemingly fearful of any movement of it. A skiagram shows a forward dislocation of the atlas upon the axis. Suggestions as to treatment are invited.

Since then an attempt has been made to reduce the dislocation by manipulation under general anaesthesia, without success.

Discussion.—Mr. PHILIP TURNER (President) said he had seen five or six cases of fractures, or fracture-dislocations, of cervical vertebrae which had not proved fatal, but he had only seen one case in a child. It was that of a boy, considerably older than the present patient, who had a severe fall from a tree. When brought to hospital his chief complaint was of pain in the occipital region and that he could not move his head. Skiagrams showed a fracture of the posterior arch of the atlas and a fracture of the odontoid process. Descriptions in books led one to expect such an injury to be immediately fatal. This boy was kept in hospital with his head between sandbags for six weeks, and at the end of that time a leather collar was made for him, and he wore that for another six weeks. He quite recovered, except that he carried his head a little on one side and its movement was deficient.

He had seen several cases of the kind in adults. One of the last he had had was due to an accident in a swimming-bath. A young man, aged 24, dived from the gallery into the shallow end of the bath, and struck the bottom of the bath forcibly. His symptoms showed there was an injury to the spinal cord; there was considerable loss of power in the legs, some loss in the arms, and very severe pain. He did not disturb the patient to enable a skiagram to

be taken, but had him kept quite still for six weeks. Under X-ray examination it was seen that he had a fracture-dislocation between the fifth and sixth cervical vertebrae. The symptoms eventually cleared up, and the patient completely recovered. In these injuries to cervical vertebrae it was possible for the patient to be free from symptoms of injury to the spinal cord at first, and yet these might appear later as the result of movement. In two cases admitted to hospital with other injuries the patients subsequently became paraplegic and died, and, post mortem, fracture of the cervical vertebrae was found. One patient, admitted for concussion, was allowed up at the end of ten days, and whilst walking about by himself he suddenly collapsed, and when picked up was found to have lost power in his arms and legs. He died shortly afterwards, and, again, fracture of the cervical vertebrae was found.

He (the President) advised that the present patient be kept immobile with the head fixed between sandbags. He thought the reason why fracture occasionally occurred in the cervical region without injury to the cord was on account of the large size of the spinal canal at that level.

Mr. B. WHITCHURCH HOWELL said that as this accident occurred nine or ten days ago, he would manipulate this case under an anæsthetic. He had seen a case which had come under observation three months after a fall from an apple tree. There was a fracture-dislocation of the cervical spine a little lower down, with subluxation of the upper fragments. He had been manipulated under an anæsthetic at two other hospitals, but without any alteration in the subluxation being produced. Stiffness of the neck became worse as the child got older, and arthritic results ensued, with neuralgic pains, and there was much incapacity later on in life.

Multiple Exostoses.

By T. PEARSE WILLIAMS, M.D.

M. R., FEMALE, aged 5 years, has been seen at intervals since November, 1922. She had measles in January, 1926.

The mother noticed small swellings on the limbs. Small firm nodules are present at the lower ends of both tibiae, the upper and inner margin of the right tibia and at the lower end of the right radius. These are not painful. There is a history of hard swellings on the arms in members of the father's family.

Discussion.—Mr. PHILIP TURNER (President) said he did not know what relation these cases bore to the condition of achondroplasia. Often the tumours were multiple and he found a number in this patient. They seemed to occur close to the epiphyseal lines, and often they were present a long time without producing any symptoms. In this case the tumours on the fingers and toes were likely to be troublesome and cause considerable disability.

As to the treatment of these exostoses, it would be noted what trouble they gave. If one of them caused disability or gave rise to symptoms, it should be removed. He did not think anything needed to be done in the case of this child at present.

Mr. B. WHITCHURCH HOWELL said he had a similar case in a girl, whom he watched for a year, and only at the beginning of this year was there trouble. The tumour was on the inner side of the tibia, at the knee, and she was knocking it. He intended to chisel away portions of it. He agreed that the present patient did not need anything done for the time being.

Case for Diagnosis (? Poliomyelitis with some Spasticity).

By D. W. WINNICOTT, M.R.C.P.

L. D., AGED 7 years, was brought up on account of a slightly abnormal gait. This has been noticed since he was about 3 years old, and has never inconvenienced him. There was no definite illness of onset.

Lower limbs.—There is slight left foot-drop. Bones: Right limb longer than left (? 2 cm.). Muscles: Right thigh circumference greater than left ($1\frac{1}{2}$ cm.). Right calf circumference greater than left (2 cm.). Power: Right foot movements,

normal power. Left foot movements, some weakness, especially inverters of foot and dorsiflexors of toes.

Vasomotor: In the cold weather the left foot was always bluer than the right, and a large chilblain had appeared on the dorsum.

Reflexes: Knee-jerks, right = left (?). Ankle-jerks, right = left. Plantars: right, definite flexor; left, indefinite extensor. Passive movement: some stiffness of the left foot movements only.

Also, X-ray of long bones shows transverse striations, symmetrical, and supposed by some to be associated with repeated illnesses. This does not appear to be the case here for the patient has had a very healthy life. They are present only in femora, tibiae and fibulae.

Discussion.—Dr. NEILL HOBHOUSE said he thought it was a case of polio-encephalitis: there had been an affection of the anterior horn cells, also probably some small hæmorrhages in the corona radiata.

Dr. REGINALD MILLER said that against Dr. Hobhouse's view was the fact that the child had not been ill. Was it to be held that in a case of congenital hemiplegia the patient should not have smaller limbs on the affected side? They would agree that this was often so. He had seen a child with hemiatrophy of the face, and one hand was so different from the other that he (the patient) called it his girl's hand; he also had a shortening of the leg. In Dr. Winnicott's case he thought there was a partial cerebral sclerosis.

Mr. B. WHITCHURCH HOWELL said he thought both this case and the next one were examples of spastic hemiplegia, and that all such cases showed a difference in the size of the limbs, particularly the upper. He considered that an extensor response was present.

Dr. A. MONCRIEFF asked what was the result of the Wassermann reaction, as this might be a syphilitic hemiplegia. Acute encephalitis seemed to be excluded and the case was not one of infantile hemiplegia.

Dr. D. W. WINNICOTT (in reply) said that the Wassermann reaction had not been tested, but the family history was against the idea of syphilis.

Case for Diagnosis (? Infantile Hemiplegia).

By D. W. WINNICOTT, M.R.C.P.

N. J., AGED 2 years 3 months, was born in difficult labour,—breech presentation, instruments being used. Afterwards the mother developed white-leg. Birth weight 10 lb.

When 8 months old he was being treated for occasional, very slight convulsions, and for minor feeding troubles, when it was noticed that he constantly held his left hand in full pronation. This the mother had noticed "for some time." On examination the left upper limb was found to be not obviously wasted, but there was paralysis of the deltoid and of the supinator group. There was some stiffness, and also it seemed at first that the child resisted passive movement because of slight pain. Under regular massage this condition improved very considerably. At that time no other abnormality was found. The child's mental and other development proceeded normally.

At the age of 1 year 5 months it was noticed that the child was not developing normal pyramidal control of the lower limbs. At that time the reflexes were found to be the following: ankle-jerks, left brisker than right; knee-jerks, left brisker than right; plantars, right, definite flexor; left, definite extensor. Later, the knee- and ankle-jerks have been found to be symmetrical, but a difference in plantar response has persisted.

When the child stands there is marked eversion of both feet, especially of the left.

The patient is forward mentally and this has helped the masseuse greatly in the task of re-educating the left upper limb.

Discussion.—Mr. B. WHITCHURCH HOWELL said he thought the pronator spasm could be diminished by a plaster splint in supination at a right angle, extending as far as possible beyond the ball of the thumb. He thought the child would get well in three years.

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Dr. NEILL HOBHOUSE said he would tie the other arm, and then he thought the signs would disappear. He would be reluctant to hamper the movements by the application of a splint.

Case of Interstitial Keratitis accompanied by Periostitis of the Tibia due to Congenital Syphilis.

By MAURICE H. WHITING, M.B., F.R.C.S.

PATIENT, P. N., aged 7 years. This is an unusual combination of congenital syphilitic manifestations. Both conditions are now quiescent.

Case of Partial Albinism.

By MAURICE H. WHITING, M.B., F.R.C.S.

PATIENT, V. A., aged 6½ years. Partial albino. First seen at age of 4½ months when there was an irregular nystagmus, translucent iris and sclera. Very fair fundus. Hair light coloured but not white. In one year development of pigment took place, so that the iris and sclera no longer transmitted the light reflex from the fundus. The hair is now brown. There is a high degree of hypermetropic astigmatism. The sight, with correction, appears to be fairly good.

Dr. E. A. COCKAYNE said he had seen a similar change occur in albinos, but never to so dark a colour as in the second case shown. Professor Karl Pearson told him that the pigment in these cases was not granular pigment, but a diffuse pigment, however dark the hair might be.

Case of Wrist-drop in a Child.

By G. A. SUTHERLAND, M.D.

S. H., MALE, aged 8 years. Admitted January 4, 1926.

Present illness.—Patient has been ill eight days. Illness began with swelling of the feet and vomiting. Blotchy red rash on feet. Constant desire to micturate. Later, severe pain in abdomen and scrotum.

On admission patient was found to be suffering from acute nephritis, right epididymitis, some swelling of ankles and a purpuric rash on the feet. Later, there were signs of right lobar pneumonia—then of left. White cell count 82,000, chiefly polymorphonuclears. Made a good recovery—convalescence interrupted by an attack of mumps. Still has albuminuria.

A month ago he was found to have left wrist-drop and this condition has persisted. There was tenderness on pressure of left forearm, but there has been no pain or tingling or numbness. Sensation was normal. There is no triceps reflex on the left side and the muscle reflex on that side is sluggish as compared with that on the right. There is perhaps slight wasting of the left forearm. The flexor muscles of the wrist are now over-active, and full extension of the wrist requires some force. The flexor muscles of the elbow are rather tense and full extension of the elbow also requires some force.

At the time the wrist-drop was noted the boy developed some weakness of the right hand. This has practically gone, with the exception that he does not flex the fore-finger of the right hand so well as the other fingers.

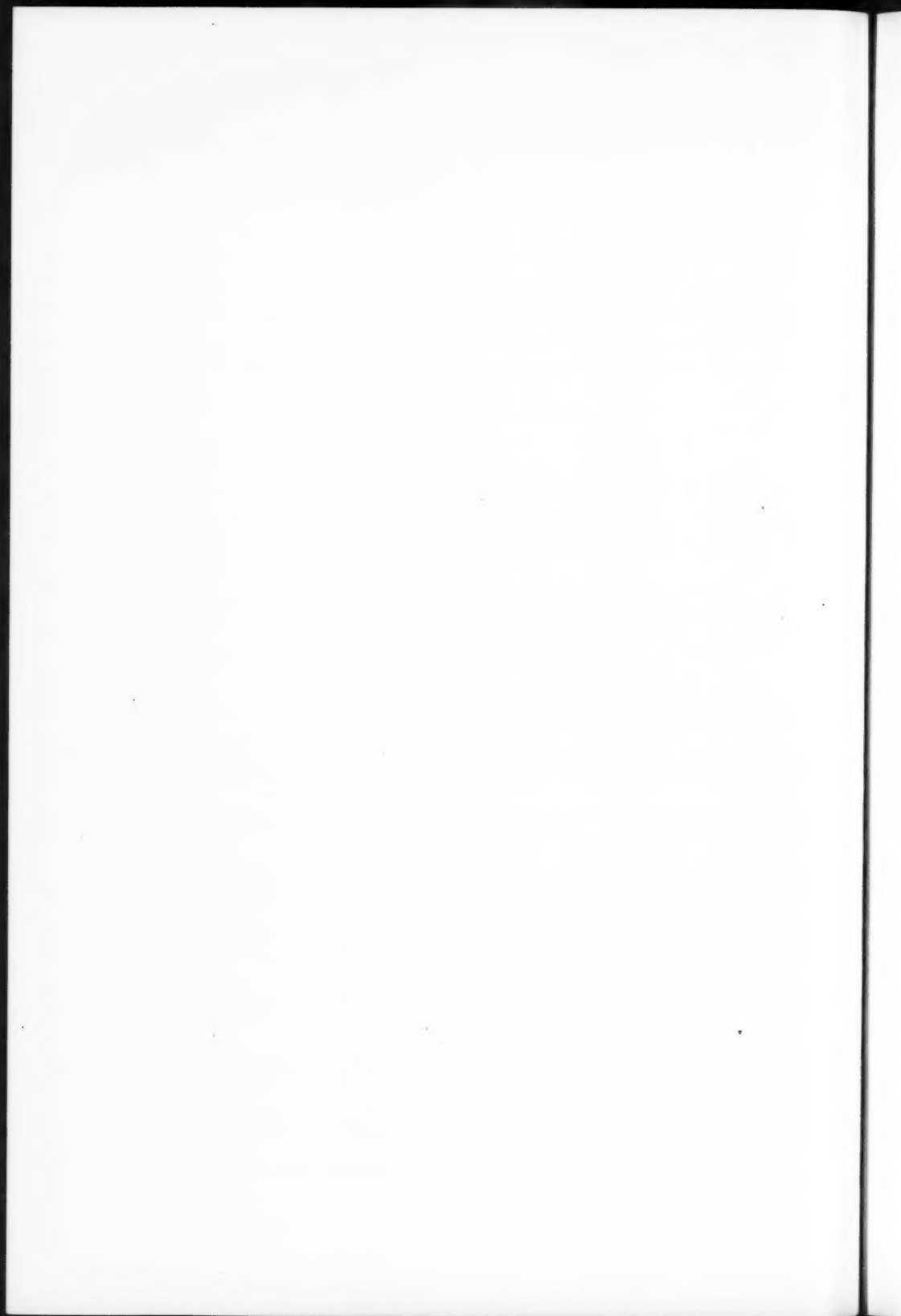
His temperament is highly neurotic.

The question is as to the cause of the wrist-drop. It was found to have arisen suddenly after a very severe infective illness. I regard it as functional paralysis, for the purpose of this discussion.

Discussion.—Dr. NEILL HOBHOUSE said he thought the reflex changes were definite, and that there was a diminution on the affected arm; it was probably organic. One possibility was peripheral neuritis, the other, poliomyelitis, preferably the former. He had not previously heard of wrist-drop in a child. During the war he saw every form of limb palsy follow the injection of quinine, and he thought that the possibility of injury to the nerve during the acute illness must be considered.

Dr. G. A. SUTHERLAND (in reply) said that he did not think the child had received any injections. Some Members had seen a similar condition after diphtheria and after typhoid fever. Probably there had been a general infection, and what was now seen was a sequel to it, in the shape of peripheral neuritis, as suggested by Dr. Hobhouse.

Dr. H. W. PERKINS gave a Demonstration of Pathological Specimens.



Section for the Study of Disease in Children.

President—Mr. PHILIP TURNER, M.S.

Case of Brittle Bones and Blue Sclerotics.

By E. A. COCKAYNE, M.D.

R. J., GIRL, aged 11 years. The father has brittle bones and has had many fractures; the mother is normal. There are four children, a brother aged 26 years with brittle bones, a sister aged 21 normal, a brother aged 20 with brittle bones, and the patient. Nothing unusual was noticed in the child until, at the age of $3\frac{1}{2}$ years, she fell and broke her right femur. This bone has been broken on three subsequent occasions, and the right and left legs were broken about four years ago. The child has been getting stout recently and was admitted to hospital for this reason. She is rather fat, especially in the mammary and pelvic regions. Sclerotics very blue; fundi normal; hearing good; teeth good. Skull normal in shape; upper limbs of average length; hands slender with tapering fingers; lower limbs small and short; the right tibia shows evidence of old fracture about midway down shaft, with union in bad position. Radiogram of skull shows pituitary fossa smaller than normal. Radiograms of limbs show multiple united fractures of the right femur and old fractures of the right and left tibiae. All the bones are very slender and rarefied; this is noticeable in the long bones and ribs and—especially—in the metacarpals. Blood-sugar: 75 mgm. per cent. before ingestion of glucose; half an hour after ingestion 173; one hour after 133; one and a half hours after 134, and two hours after 149 (mgm. per cent.). Sugar tolerance slightly increased. For the sugar-tolerance test I am indebted to Professor E. C. Dodds, and for the radiograms to Dr. Nicholas.

I think she has a slight degree of hypopituitarism.

Discussion.—Dr. DONALD PATERSON suggested that the blood-calcium content should be ascertained. In one of his (the speaker's) cases of this disease he had had the blood-calcium tested and it was normal, therefore there had been no necessity to adopt anti-rachitic treatment, such as artificial sunshine and feeding with fat-soluble vitamins. At Copenhagen, in September, he (Dr. Paterson) had heard that cases were being treated with injections of goat serum; and in Austria, recently, a paper had been published claiming that by Bier's congestion method the bones could be made to calcify.

Mr. PHILIP TURNER (President) asked what the patient was doing at present. If she was getting about, to what extent did she do so? Obviously she was very heavy, and the skiagrams showed, what indeed was evident on merely feeling the bones, that the bones were extraordinarily slender, so slender that, even if they had not a brittle character, they would conceivably fracture easily.

Dr. COCKAYNE (in reply) said that he did not see how any treatment was likely to make thin bones thick. In answer to the President he said that the girl was unable even to stand up, and she seemed afraid of trying to support her weight. She had therefore remained in bed, and he felt sure that now that she had grown stout, if she were to attempt to walk, a fracture would soon occur.

Congenital Syphilis: Cirrhosis of Liver.

By E. A. COCKAYNE, M.D.

R. B., BOY, aged 10 years. Only child. Past history and family history *nil ad rem*. First became jaundiced at the end of December, 1925; the jaundice has disappeared twice but returned again. Has felt well and eaten ordinary food with appetite; has had no pain. No change noticed in the colour of the fæces. Weight 4 st. 3 lb. (normal for age 4 st. 4½ lb.); height 4 ft. 4 in. On admission to hospital the boy looked well but was moderately jaundiced. Features well formed, teeth normal. Liver four fingers' breadth below costal margin; firm but smooth; not tender; spleen two fingers' breadth below costal margin; no ascites. Fæces normal in colour. Urine contained bile-pigment and bile-salts, and urobilin and urobilinogen were present in excess; diastase 40 units. Blood count: 5,120,000 red cells and 6,400 leucocytes per c.mm.; hæmoglobin 80 per cent.; colour index 0·8; fragility of red cells normal; hæmolysis in 0·45 per cent. NaCl. Blood serum: Fouchet's test positive; van den Bergh's test indirect positive. Cholesterol 105 mgm. per cent. Blood urea 24, non-protein nitrogen 27, creatinin 1·9, uric acid 2·4, amino-acid nitrogen 5·0, and sugar 98 mgm. per cent. (Normal figures.) Wassermann reaction positive. Galactose tolerance (30 grm.); blood-sugar: before ingestion 64 mgm. per cent.; half an hour after 144; one hour after 152; an hour and a half after 182; and two hours after 133 (mgm. per cent.); urine contained 5·5 gr. of galactose. Carbohydrate function of liver inefficient. Except the cirrhosis of the liver the boy shows no signs of congenital syphilis. For the biochemical investigations I am indebted to Professor E. C. Dodds.

Catarrhal jaundice very seldom recurs twice, and rarely recurs at all. Although the Wassermann reaction was positive, I did not suspect syphilis. I should like opinions as to whether this is pericellular cirrhosis, or multilobular cirrhosis. Dr. Parkes Weber has described recurring jaundice in syphilitic children, in which the liver was affected with multilobular cirrhosis. The boy's liver is smooth, and I am inclined to regard this case as one of late pericellular cirrhosis.

Two Cases of Post-encephalitic Hyperpnœa.

By D. W. WINNICOTT, M.R.C.P.

W. B., AGED 7 years, was brought in February, 1925, to the Queen's Hospital for Children, because of attacks of exaggerated breathing. The child was healthy till an illness in his fourth year. He was suddenly taken ill, screamed all night, was quite violent and was restrained with difficulty. A doctor was called in and at first diagnosed chorea, but later said it was not chorea. (This doctor has unfortunately died.) After one week the patient became excessively sleepy and could not be awakened. For some months afterwards he was less restrained than formerly and very sleepy during the day. At that time he had an abscess in the groin.

When about 5 years old he developed the attacks of exaggerated breathing of which he now complains. There have been no paralyses nor are there any residual signs. His intelligence is nearly normal. Lately there has been a return of sleepiness in the day. He is now liable to strong passions lasting about twenty minutes, and during these outbreaks he may do anything.

D. T., aged 3 years, was healthy until April, 1925, when she had an illness thought to be measles, followed by mumps. During the "measles" the child slept almost all the time during the first fortnight.

In July, 1925, she was brought to the Queen's Hospital for Children because she had had reversed sleep rhythm since the illness in April. Also she had frequent

night terrors, or a woke from sleep twitching. Occasionally there was twitching in the day. No paralyses were found.

In September, 1925, she began to have attacks of exaggerated breathing, lasting about ten minutes with about half-hourly intervals. These had been diagnosed by a doctor as attacks of asthma.

In October, 1925, the child was an in-patient for a fortnight, and had no attacks until her mother came to fetch her. At the present time there remains reversed sleep rhythm, night terrors have returned, and attacks of exaggerated breathing occur several times an hour. No alteration in mentality has been noticed and intellectual development has proceeded normally.

Discussion.—Dr. WINNICOTT said he went into the question of what brought on the exaggerated breathing, thinking it might be hysterical. He was able to investigate the boy to some extent, because he was very fond of drawing, and would draw everything which came to his mind. There were certain ideas which were, to him, taboo, and whenever he approached them this exaggerated breathing would begin, evidently part of an expression of fear.

In the little girl the fast breathing seemed to have no relation to ideas. It persisted practically all day, except when she was asleep, and the attacks lasted perhaps ten minutes, with a five-minutes interval. A third, more typical case of encephalitis lethargica followed by exaggerated breathing could not be shown because the patient had been admitted to a hospital.

Dr. G. A. SUTHERLAND said that Dr. Winnicott was fortunate in having had three cases of this condition under his care, as they could not be very common; he (the speaker) had not himself seen any. The diagnosis that it was a post-encephalitic condition was probably correct, at least it was very plausible. If the initial illness in the second case had been measles, this might have been followed by cerebral complications. It was interesting to note the type of breathing; he only saw it in the second case, as it was not in action in the boy. In the girl the breathing was of the thoracic type, and apparently there was not any involvement of the respiratory centre of the medulla. The abdominal breathing appeared to be normal. He (Dr. Sutherland) concluded, therefore, that it was the upper nervous centres which were involved in this case. It was the type of breathing assumed when under excitement or in distress; if there was a call for increased breathing, it was done through the thoracic muscles, not through the diaphragm. The idea was supported by the fact that the quick breathing was not present during sleep. It was interesting to hear that the original diagnosis in one of the cases was hysteria or a functional disorder, because there had been a tendency to attribute the sequelæ of encephalitis lethargica to a hysterical condition. That was so in some cases of choreiform movements which he (the speaker) had seen, as the sequelæ of encephalitis.

Dr. E. STOLKIND said that, according to the history, both cases, and especially that of the first child of seven years, with excessive sleepiness, were in all probability cases of post-encephalitic hyperpnœa. Such cases were not infrequently diagnosed as hysterical. During the acute stage, as well as later, various changes in the respiratory rhythm had been observed. In some cases tachypnœa occurred, in others bradypnœa or apnœa, &c. This phenomenon might last for days or for many months.

Dr. WINNICOTT (in reply) said that he did not intend to convey the idea that the encephalitis had been mistaken for mumps. He thought the child had mumps after having had either measles with encephalitis, or encephalitis diagnosed as measles. Several cases had been published in which encephalitis had complicated measles, and in some of these cases there were sequelæ.

GENERAL REFERENCE: Turner and Critchley, *Brain*, 1925, pt. 1, p. 72.

Case of Congenital Œdema of the Feet.

By H. CHODAK GREGORY, M.D.

BABY girl, aged 5 months. Full-time child, normal confinement. Both feet were noticed to be œdematous at birth. Œdema persisted. When the infant was two weeks old the urine contained a moderate amount of albumin, but several

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specimens have been tested since and found free from albumin. The œdema has never spread, and occasionally disappears temporarily; it is worse in the mornings. Wassermann reaction negative.

As to the cause, I suppose there is some malformation of veins, or lymphatics, or both, and so the circulation is retarded. I think the prognosis is good; in most cases the patients recover, because a collateral circulation is probably established.

Discussion.—Dr. W. M. FELDMAN said that as a trace of albumin was found when the infant was two weeks old, the condition might not have been due to starchy food. Albuminuria in babies was common.

Dr. E. A. COCKAYNE asked whether Dr. Gregory had considered the possibility of this being a case of Milroy's disease. There was no family history, but that was not necessary in those cases. If it was Milroy's disease, the œdema might be expected to increase.

Dr. CHODAK GREGORY (in reply) said that the baby had been breast-fed, but even if that had not been the case, it had been born with the œdema, therefore feeding did not enter into the question. She (Dr. Gregory) understood that Milroy's œdema was a non-pitting œdema, though there did not seem to be unanimity of opinion on this point. In the only case of Milroy's œdema which she had seen the œdema had extended up the leg and thigh.

Case of Juvenile Parenchymatous Neuro-syphilis.

By NEILL HOBHOUSE, M.B.

J. R., AGED 9 years. Brought to hospital for incontinence of urine. No other symptoms.

The parents are dead, and no accurate family history can be obtained. The mother had about thirteen children, and probably some miscarriages. Only three of the children are alive now; one is a deaf-mute. Most of the others died in infancy.

There are very few physical signs; inactive pupils without paralysis of accommodation. The right knee-jerk is usually, but not always, more brisk than the left. There is a tendency to pes cavus. A certain degree of incontinence of urine is present.

Wassermann reaction of blood + +.

Cerebro-spinal fluid. Wassermann reaction + +. Cells 60 per c.mm.

Lange: 2344321000. Globulin in slight excess.

This appears to be a very early stage of parenchymatous syphilis, probably a precursor of juvenile tabes or G.P.I. Treatment with injections of sulfarsenol has been begun.

My experience of the treatment of juvenile neuro-syphilis has not been fortunate, but I have not seen another case which has been placed under the treatment so early in the disease, and I feel more hopeful about this one. I have begun with 0.36 grm. of sulfarsenol, and if it is tolerated I shall increase the dose fairly quickly.

Discussion.—Dr. V. S. HODSON asked if Dr. Hobhouse had considered the possibility of treating the child by malaria.

Dr. NEILL HOBHOUSE (in reply) said that he did not think the indications that it was a precursor of G.P.I. were strong enough to justify treatment by malaria. He would like to have the Lange curve repeated before undertaking that treatment.

Case of Fibrillation of the Abdominal and Shoulder-girdle Muscles (? Progressive Muscular Atrophy) as a Sequel of Poliomyelitis.

Shown by W. G. WYLLIE, M.D. (for DONALD PATERSON, M.B.).

BOY, aged 11 years; when eighteen months old he had an illness, with convulsions, said to be meningitis, but the type of meningitis was not ascertained. After this "his head dropped right back and he was unable to sit up." He gradually recovered power to walk, but "was only able to get up a kerb on his hands and knees."

At the age of four years he had measles and pneumonia, and again went off his feet. He became very thin, and scoliosis of the spine developed rapidly, so he was placed on a back-board for two years, and the spinal deformity disappeared. He regained the power of walking. In 1925 he had herpes zoster round the waist. During the last nine months flickering of the abdominal and shoulder-girdle muscles has been observed, the scapulæ have become winged, and he has not been able to sit up so well as formerly.

The fibrillation is not very well shown this afternoon. Usually there has been intense fibrillation of all the abdominal muscles, and those of the shoulder-girdles. It is most likely he had suffered from poliomyelitis, because on recovery he could not hold his head up, and he was very weak. It took him a long time to walk, and in order to go up even one step he had to crawl on his hands and knees. He afterwards developed kyphosis, and had to lie on a back-board for two years. Progressive muscular atrophy is known to supervene after poliomyelitis, but the earliest age at which I have seen such a case occur has been 18 years. The child is now aged 11 years.

Dr. G. A. SUTHERLAND agreed that the fibrillation was not very well seen to-day, and he asked which part of the muscle was fibrillating. Was it that portion which had been completely destroyed, i.e., which had been cut off from its nervous control, or was it taking place in the parts in which there still remained some nervous control? Experimental work had shown that if the nerve supplying a muscle were divided, that muscle went into a state of fibrillation. He believed that in the present case the muscles or parts of muscles which fibrillated were those which had been completely deprived of nervous control. Was it necessary to assume the agency of another factor, such as progressive muscular atrophy? He thought the whole condition was due to the anterior poliomyelitis.

Case of Splenic Anæmia (Banti's Disease).

Shown by J. PEARCE (for DONALD PATERSON, M.B.).

J. S., AGED 6 years, female.

Family history.—The fifth of seven children, the father and mother and other children alive and healthy.

Past history.—Full-time baby, "born black," with "heart disease." Measles, January, 1924. In May, 1924, three days of hæmatemesis with black stools. August, 1924, diphtheria, nasal discharge since then.

History of present condition.—Child was seen as an out-patient on July 13, 1925, for nasal discharge. Plump, pale, nutrition good, tonsils moderately enlarged, postnasal catarrh, no abnormality in lungs, heart enlarged (confirmed by X-ray), soft systolic murmur at apex, abdomen full and soft, no enlargement of liver or spleen, urine normal. Weight 2 st. 13 lb. 10 oz. The nasal condition improved but on October 12 she was brought to hospital because she had "vomited a pint of blood and passed blood in her stools." She was admitted to Westminster Hospital. Her temperature was 99.4° F. No abnormal physical signs, except the enlarged heart and systolic murmur; no source of hæmorrhage was found in nose or throat, and the skiagram of an opaque meal showed no abnormality of the stomach. Her stools were positive for occult blood. Blood-count: Red blood-cells 3,910,000; hæmoglobin 74 per cent.; colour index 0.8; white blood-cells 7,860 (polymorphonuclears 65 per cent., monomorphonuclears 35 per cent.); Wassermann reaction negative. The child improved and was temporarily discharged on November 1. At no time was the spleen found to be enlarged. She had a further small hæmatemesis on November 13, and when seen on November 23 was very pale and bloodless. On January 4, 1926, the spleen was found to be palpable and on January 6 she was readmitted.

The heart condition remained as before, the liver was not enlarged but the spleen was felt 2 in. below the costal margin. Her blood now gave the following count: Red blood-cells 4,750,000; hæmoglobin 74 per cent.; colour index 0·8; white blood-cells 6,400 (polymorphonuclears 65 per cent., monomorphonuclears 35 per cent.); no change in nature or shape of red blood-cells; complete hæmolysis of red blood-cells occurred in 0·3 per cent. NaCl, partial in 0·4 per cent., *nil* in 0·5 per cent. On January 25 the blood-count was: Red blood-cells 4,360,000; hæmoglobin 65 per cent.; colour index 0·75; white blood-cells 6,000 (polymorphonuclears 35 per cent., monomorphonuclears 65 per cent.).

On February 18 the spleen was removed by Mr. Carling. On the two days following this there was vomiting of blood and coffee-ground material; since then there has been no recurrence.

On February 22 the blood-count was: Red blood-cells 5,940,000 per c.mm.; hæmoglobin 80 per cent.; colour index 0·7; white blood-cells 13,400 per c.mm. (polymorphonuclears 60 per cent., monomorphonuclears 40 per cent.).

On March 12: Red blood-cells 4,730,000; hæmoglobin 70 per cent.; colour index 0·74; white blood-cells 8,600 (polymorphonuclears 59 per cent., monomorphonuclears 41 per cent.); complete hæmolysis in 0·2 per cent. NaCl, partial in 0·3 per cent.

She was discharged from hospital on this date, the abdominal wound having healed without any complication.

Seen on March 18 her weight was 3 st. 5 lb., a gain of more than 5 lb. since July, 1925.

SUMMARY OF BLOOD EXAMINATIONS.

	R.B.C.	Hgb.	C.I.	W.B.C.	Poly.	Mono.
October 19, 1925	3,910,000	55 per cent.	0·7	7,860	70 per cent.	30 per cent.
January 7, 1926	4,750,000	74	0·8	6,400	65	35
January 25, 1926	4,360,000	65	0·75	6,000	35	65
February 22, 1926	5,940,000	80	0·7	13,400	60	40
March 2, 1926	6,000,000	70	0·63	8,200	60	40
March 12, 1926	4,730,000	70	0·74	8,600	59	41

FRAGILITY OF CORPUSCLES.

	Complete.	Partial.	Nil.
January 7, 1926	0·3 per cent.	0·4 per cent.	0·5 per cent. NaCl
March 12, 1926	0·2	0·3	0·4

REPORT ON SPLEEN BY DR. BRAXTON HICKS, PATHOLOGIST.

"A spleen weighing 10 oz., very firm and pale brown on section.

"*Histology*.—A well-marked increase of all the fibrous tissue elements of the spleen. The bulk of the lymphoid tissue appears to have disappeared, and thus the reticulum, aided by the fibrosis which has occurred, becomes very prominent and resembles the interstices of a sponge. The spaces are filled with blood. There is no resemblance to the type of spleen seen in the classic 'Gaucher's anæmia,' but the changes are exactly similar to those I have seen in practically all other types of 'splenic anæmia.'"

Discussion.—Dr. DONALD PATERSON reminded Members of specimens he showed at the January meeting of the Section, from what was, he thought, accepted by most as a case of Banti's disease.¹ It was the case of a boy, aged 3½ years, who was admitted with a large spleen and anæmia, and he had a large hæmatemesis; he died. The patient was under the care of Dr. Poynton. The post-mortem examination revealed a large fibrotic spleen, and at the lower end of the œsophagus there were a number of varices, from which a clot of blood could be seen emerging. Evidently that had been the site of the bleeding. He suggested that in the case of the present child there were varices in the stomach or the lower end of the œsophagus, and that the bleeding on the two occasions came from there. In the instance of the child now shown there was no comparison, since the spleen had been removed with the former condition. Previously she had never looked robust, and for a number of years she had been a good deal in and out of hospital; now, she was greatly improved in health. He could not account for the slight drop in the red and white cells, except upon the assumption that this was due to

¹ *Proceedings*, 1926, xix, p. 39.

her having been out of the sun a good deal and having become somewhat hospitalized. But now that she had returned home she might get still better.

Dr. W. M. FELDMAN asked whether the exhibitors did not think the apparent drop in the proportion of red cells might be due to an increase in the volume of blood. There might actually be an increase of cells.

Dr. J. PEARCE (in reply) said that he thought Dr. Feldman's suggestion was a probable explanation of the decrease in the number of corpuscles. The question now was whether, the spleen having been removed, the varices which were presumed to be present would disappear, i.e., whether, in the future, the child would be free from attacks of hæmatemesis.

Case of Pyloric Stenosis (Pylorospasm).

By W. M. FELDMAN, M.D.

IF this is pyloric stenosis, it is a rare condition in a girl. And the question arises as to what is the nature of the stenosis. This baby was brought into the hospital when it was two or three weeks old. She was breast-fed. She had all the symptoms typical of pyloric stenosis, namely, vomiting after each feed, and I think there has been seen some peristalsis in the stomach, though no lump could be felt. As the baby did not improve under ordinary medical treatment, such as lavage, the giving of carbohydrates and the restriction of the amount of the food taken at a time, I asked my surgical colleague, Mr. Loughnane, to operate. The operation was done, but no pyloric stenosis was found, and the abdomen was closed up again. The patient continued to go downhill. I tried the effect of giving 1000 gr. atropine after each feed, and for a time after that the vomiting ceased. The infant still wasted; I therefore decided to put her on thick feeds, and she put on weight. I show the weight chart, the readings of which bear out the uninterrupted rise in weight after the thick feeds had been begun. At birth the child weighed 5½ lb.; she now weighs between 11 and 12 lb. If there was pyloric stenosis, it was of the spasmodic kind, and in that case the stenosis would not be visible at operation. I tried thick feeds, as their use has been extolled not only in Germany, but also in France. It seems that they act by giving the stomach some definite volume to work upon, and so enable it to drive its contents through the pylorus into the duodenum. Recently a paper appeared in the *British Medical Journal* on the subject by an author who went to Germany and studied the effects of thick food there; his conclusion was that thick feeds do not show any marked improvement over any other kinds. But in this particular case it seems to have done wonders.

The actual composition of the thick food on which the baby was put about a month after the operation was cows' milk 3 iv, water 3 iv, mabela 5 i ss. The mixture was boiled for fifteen minutes to reduce it to 3 vi. Small quantities of this, starting with one ounce, were given at frequent intervals, and as the baby began to thrive, the amounts, as well as the intervals, were gradually increased.

Discussion.—Dr. E. A. COCKAYNE suggested that the title of the case should be altered to that of "pylorospasm." He asked whether true peristalsis was really seen, as it was very rare for it to be visible in cases of pylorospasm. In the latter condition, he had seen the stomach stand up, but had not seen waves of peristalsis cross it.

Dr. W. M. FELDMAN replied that of course the title should be changed to "pylorospasm." He had not personally seen any peristalsis in the case; he was merely relating what was told to him at the time by the house physician.

Case of Tuberous Sclerosis.

Shown by Miss DILYS JONES (for DONALD PATERSON, M.B.)

A. W., AGED 13½ years. First seen by Dr. Paterson in the Out-patients' Department of Westminster Hospital on October 15, 1925.

Complaint.—Headaches and attacks of vomiting for three years. Failing vision for seventeen months. He has had a red rash on his face all his life (fig. 1). At the age of 10 years his tonsils were removed, and since then, i.e., for three years before examination, he had had frequent attacks of headache and vomiting.



FIG. 1.

At 12½ years, i.e., twelve months previously, he had an attack of gastritis, and was in bed for two months, with pains in his head and stomach, and vomiting. From this time the vomiting continued until he was admitted to hospital on November 3, 1925, but the headaches occurred only in the morning. From the same time also, his eyes were noticed to become more prominent, and his eyesight began to fail. He attended school until July, 1925, when he had another attack of sickness and headache and was in bed for six weeks.

Past illnesses.—Measles, whooping cough.

Examination.—(Skin report by Dr. Dore.) Adenoma sebaceum, a well marked case of the vascular type. A developmental condition showing hypertrophy of sebaceous glands, and hyperplasia of capillaries.

(Eye report by Mr. Arthur Griffith.) Eyes prominent, with diminution of abduction in each. Right eye: fingers seen at one metre. Left eye: fingers seen at two metres. Papilloedema of both discs and central choroido-retinitis.

November 3, 1925.—Admitted to Sir James Purves-Stewart's ward for further examination.

Pupils moderately dilated, react to light and accommodation. Optic disc swollen. Other cranial nerves normal. Teeth good. Small papilloma over upper right lateral incisor. Tongue clean. Heart and lungs normal. Upper limbs: grasps strong and equal. Lower limbs: no motor weakness; gait, that of a blind man.

Reflexes.—Knee-jerks, normal. Ankle-jerks, just present; no ankle clonus.



FIG. 2.

Plantar reflexes: flexor. Abdominal reflexes: both lower present; upper not elicited.

November 3, 1925.—Triple puncture performed. Fluid not under pressure. Ventricle fluid slightly pigmented, lumbar fluid paler. Since then patient has had no headache.

November 10, 1925.—Double ventricle puncture performed. 160 c.c. of air were introduced into the left ventricle, and a corresponding amount of cerebro-spinal fluid withdrawn from the right (fig. 2).

Pneumoradiograms show enormous dilatation of the left lateral ventricle. He vomited twice on the following day, but since that has had no headache or vomiting

60 Dilys Jones : *Tuberous Sclerosis*; Paterson : *Familial Microcephaly*

up to the present. His eyesight has continued to fail and is now limited to perception of light in each eye.

Pathological reports :—

Blood : Wassermann reaction negative. Cerebro-spinal fluid : Wassermann reaction negative. Gold curve : 000000000.

	Ventricle	Cistern	Lumbar
Lymphocytes ...	6·7 per c.mm. ...	Less than 1 ...	4 per c.mm.
Globulin ...	Marked positive ...	Marked positive ...	Marked positive
Albumin ...	0·3 per cent. ...	0·18 per cent. ...	0·14 per cent.

Dr. DONALD PATERSON admitted that unless one had a section of one of the nodules under the microscope, the diagnosis was open to doubt; it must be assumed that, the boy having a cerebral tumour and adenoma sebaceum, it was likely to be tuberous sclerosis. The question was whether the diagnosis could ever be made during life.

A point which Dr. Dilys Jones had not mentioned was that these little tumours were found in all the organs, and sometimes caused symptoms elsewhere. This child seemed to be otherwise sound, and that might be considered to be a point against the condition being tuberous sclerosis.

Case of Familial Microcephaly.

By DONALD PATERSON, M.B.

THE elder of the two children is aged $3\frac{1}{2}$ years—circumference of his head 17 in. In the younger, a girl aged 6 months, the circumference of the head is $13\frac{1}{2}$ in.

The elder is a well marked case of microcephalic idiocy. The younger is also a microcephalic idiot, although the intelligence she shows promises to be superior to that of her brother.

There has been one male between the birth of these two children who died at the age of 4 months and who was said to be a normal infant.

There have been no miscarriages and the Wassermann reaction is negative.

The mother's age is 25, that of the father 32. They are apparently perfectly healthy and normal. There is no history of microcephaly or idiocy on either side of their families.

This is a case in which a woman gave birth to two microcephalic idiots. I have never seen such an occurrence before. I have been in the habit, as others have, of assuring the mother of a microcephalic idiot that she would probably never give birth to a second idiot, but this occurrence shows that such an assumption may be wrong.

Discussion.—Dr. E. A. COCKAYNE said he considered it was a rash statement to make to mothers that they would not give birth to another microcephalic infant; the literature showed a number of pairs of such children in a family. He showed two of them in a family to the American physicians during their visit to this country. The first of them, born of quite healthy parents, was even more markedly microcephalic than these now shown, and the second one more so still. He thought microcephaly was in some instances a Mendelian recessive; familial cases were too numerous to be a mere matter of chance.

Dr. W. M. FELDMAN agreed that it was rash to promise a mother she would not give birth to a second microcephalic idiot; nothing was impossible in medicine. Even without invoking the law of Mendelian recessives, there was always the chance that a similar defective infant might be produced.

Dr. DONALD PATERSON (in reply) said he was surprised that other instances of the kind had been seen so commonly. He had seen microcephalic twins, but never before two of that kind at separate confinements in the same family. Notwithstanding what Dr. Cockayne said, he thought they must be extremely rare occurrences; he questioned whether anyone else in the experienced audience besides Dr. Cockayne had seen them at separate births in the same family.

Section for the Study of Disease in Children.¹

President—Mr. PHILIP TURNER, M.S.

Enlargement of Liver: Case for Diagnosis.

By R. RILEY, L.R.C.P.Lond., M.R.C.S.Eng. (for ROBERT HUTCHISON, M.D.).

BOY, aged 10 years. Admitted February 24, 1926, with a history of abdominal pain, commencing six weeks before admission, and occurring about twenty minutes after food. During this time he had had three slight attacks of jaundice. There has been no vomiting, and the bowels have been regular.

Condition on Admission.—Patient is thin. There are a few small glands palpable in the right axilla and in the neck. The liver is enlarged, especially the left lobe, which extends nearly halfway to the umbilicus, and is firm and irregular. The spleen is just palpable. Wassermann reaction negative. Blood-count shows: red blood-cells, 6,072,000 per c.mm.; hæmoglobin, 62 per cent.; white blood-cells, 15,900 per c.mm.; polymorphonuclears, 64 per cent.; lymphocytes, 34 per cent.

Tremor: Case for Diagnosis.

By R. RILEY, L.R.C.P.Lond., M.R.C.S.Eng. (for ROBERT HUTCHISON, M.D.).

GIRL, aged 8 years 10 months. Admitted to hospital March 8, 1926, for a general tremor which has been present since infancy. Nothing abnormal during pregnancy or labour. Has had no previous illness. Did not walk until she was 3½ years.

She is unusually bright and very fidgety. Movements affect whole body. No nystagmus. All reflexes are brisk. No signs of organic nervous disease. Discs normal. Head circumference 19½ in. Wassermann reaction negative.

Two Cases of Congenital Familial Cirrhosis of the Liver.

By W. P. H. SHELDON, M.D. (for F. J. POYNTON, M.D.).

A. B., AGED 9 years, and O. B., aged 4 years, brother and sister. In both, the enlargement of the abdomen has been present since birth.

A. B. has been under observation for six years. When first seen the liver extended down to the umbilicus, the spleen was not palpable, and there was no ascites. The heart was slightly dilated, an apical systolic murmur audible. Blood examination showed red blood-cells 4,900,000; white blood-cells 10,600; polymorphonuclears 50 per cent.

A year later an attack of jaundice occurred and was accompanied by enlargement of the spleen. With the disappearance of the jaundice the spleen ceased to be palpable. Since then there have been occasional severe attacks of epistaxis.

¹ Clinical Meeting at the Hospital for Sick Children, Great Ormond Street, W.C.1, Friday, April 23, 1926.

Present Condition.—Height 41 in., weight 44 lb. Liver extends down to the right iliac crest. Spleen not palpable. No ascites.

O. B. has been under observation for twenty-one months. When first seen, the liver reached the level of the umbilicus. Spleen just palpable. No ascites. Blood examination showed red blood-cells 4,500,000; white blood-cells 19,688; polymorphonuclears 50 per cent. Except for a brief attack of jaundice in 1922, both jaundice and hæmorrhages have been absent.

Present Condition.—Height 36 in., weight 31 lb. Well-marked telangiectases upon the cheeks. Liver extends down to level of the umbilicus. Spleen not palpable. No ascites.

In both cases the blood fragility was found to be normal. Van den Bergh's and the levulose tests were also normal.

Wassermann reaction of both patients was negative.

Both cases have been recorded by Dr. Poynton and Dr. W. G. Wyllie in *Archives of Disease in Childhood*, 1926, i, p. 1.

Polyarthrititis with Scleroderma.

By G. F. STILL, M.D.

BOY, aged 6½ years. Healthy until May, 1924. First came under observation in September, 1924, when the hips, knees, shoulders and elbows were swollen and painful. This condition had been present for five months. The heart was found to be displaced to the left. Next under observation in May, 1925; by that time the wrists and finger-joints had become swollen.

Present Condition.—Limitation of movements of all the joints of the arms and legs except the feet. Scleroderma especially marked in the skin of the limbs. Heart displaced to the left, the left border extending fully two fingers' breadth beyond the left nipple. Spleen not palpable. Temperature normal.

Syphilitic Pseudo-Osteo-arthritis.

By G. F. STILL, M.D.

BOY, aged 5½ years. Second child; no miscarriages. First came under observation two years ago, with spindle-shaped swellings of interphalangeal joints of all fingers (photograph shown), also interstitial keratitis. X-ray showed periarticular thickening, but no bone changes. Wassermann reaction strongly positive.

The patient has had no arsenical preparations but has received continuous treatment with mercury (hyd. cum cret.), and there is now practically no trace of the arthritis.

Polyarthrititis with Enlargement of Lymph Glands.

By R. HUTCHISON, M.D.

GIRL, aged 5 years. Swelling of joints began two years ago. She now shows swelling of elbows, wrists, fingers, knees and ankles. Epitrochlear and axillary lymphatic glands enlarged. The spleen is not palpable.

Two Cases of Cardiospasm.

By G. F. STILL, M.D.

Case I.—Boy, aged 2 years. History of vomiting on and off "since birth." Vomits immediately after taking solid food.

Patient's uncle suffered in exactly the same manner from infancy until the age of 14.

X-ray photograph shows delay in passage of opaque fluid into stomach, with dilatation of œsophagus.

Case II.—Girl, aged 4 years. History of vomiting at least once a day since birth, the vomit consisting of unaltered food.

X-ray photograph shows obstruction to passage of barium at cardiac end of œsophagus.

Cardiospasm.

By F. J. POYNTON, M.D.

GIRL, aged 9 years. History of vomiting after taking solid food since the age of 11 months. X-ray shows obstruction to passage of barium in lower part of the œsophagus. Condition improved by the passage of bougies.

Generalized Tremor, commencing in Infancy.

By W. J. PEARSON, D.S.O., M.C., M.D.

N. L., GIRL, aged 10 years, was first noticed to be shaky in all her movements at the age of 3½ years. Tremor is present on standing, but becomes more obvious on walking and in all voluntary movements of the limbs. Up till recently, in writing she steadied the right hand by holding it with the left.

She was born at full term, breech delivery, no instruments. She is the youngest of several children, but was born fourteen years later than the child next to her in age. As a baby she was unusually quiet and slept a great deal. She learnt to walk and talk at the normal age-time, but has always talked slowly.

Examination: Discs normal, nystagmus absent, knee-jerks ++, ankle-jerks +, superficial abdominals present, plantars flexor. Muscular power good, sensation normal. Intelligence fair.

Midget.

By R. S. FREW, M.D.

GIRL, aged 3 years 10 months. Only child. Birth weight, 5 lb. Present weight, 15 lb. Height, 24½ in. Mother's height is 5 ft. 1 in., and the father is 2 in. taller.

Spring Catarrh.

By P. G. DOYNE, F.R.C.S.

PATIENT, a boy, aged 10 years. The lower lids appear milk-like, the upper lids show well-marked mosaic-like excrescences. Condition worse during summer; improves in the winter months.

Congenital Glaucoma.

By P. G. DOYNE, F.R.C.S.

PATIENT, a boy, aged 4 years. Both eyes show large corneæ. The discs are atrophic and cupped. There is nystagmus, and the tension is raised. Vision less than $\frac{6}{60}$.

Ocular Torticollis.

By P. G. DOYNE, F.R.C.S.

PATIENT, a girl, aged 6 years. Face hemi-atrophied. Right hyperphoria. On an attempt of the patient to straighten the head, the right eye turns upwards, the left downwards. When looking to the left, the right eye again turns upwards and the left downwards. No diplopia.

Operation.—Tenotomy of right superior oblique.

Result.—The head is now held straighter when the body is tilted.

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SESSION 1925-26

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**SECTION OF DERMATOLOGY WITH THE SECTION
FOR THE STUDY OF DISEASE IN CHILDREN.**

(JOINT DISCUSSION No. 5.)

December 17, 1925.

**DISCUSSION ON THE ÆTIOLOGY AND TREATMENT OF
INFANTILE ECZEMA.**

Dr. A. M. H. GRAY (pp. 71, 83), Dr. H. C. CAMERON (pp. 74, 83), Dr. H. G. ADAMSON (p. 77), Dr. F. LANGMEAD (p. 78), Dr. J. M. H. MACLEOD (p. 79), Dr. G. H. LANCASHIRE (Manchester) (p. 80), Dr. HALDIN DAVIS (p. 80), Dr. MURRAY BLIGH (Liverpool) (p. 81), Mr. FRANK COKE (p. 82), Dr. S. E. DORE (p. 82), Dr. M. SYDNEY THOMSON (p. 82), Dr. J. H. SEQUIRA (Chairman), (p. 83).

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

LONDON:

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Section of Dermatology.

President—Dr. J. H. SEQUEIRA.

Case for Diagnosis (Parapsoriasis).

By J. H. SEQUEIRA, M.D. (President).

THE eruption consisted of scattered plaques, some of diffuse erythematous type with slight scaling, others of reticulate character associated with a moderate increase in the proportion of lymphocytes, without material change in the total number of leucocytes. The patient is a young man aged 27, otherwise in good health.

Case of Kaposi's Multiple Idiopathic Pigment Sarcoma.

By J. H. SEQUEIRA, M.D. (President).

THE patient has been seen by the Members of this Section on several occasions since 1913. He is now exhibited because on the front of the right leg the eruption—proved by biopsy to be of the usual hæmorrhagic granulomatous type—has, during the past year, developed a large fungating nodular tumour. The leg (shown) has been amputated, and sections of the tumour show that it is now a round-celled sarcoma. The case will be described fully in an early number of the *British Journal of Dermatology*.

Case of Lupus Erythematosus affecting Covered Parts of Body.

By A. C. ROXBURGH, M.D.

B. S., MALE, aged 34. Eighteen months ago had lupus erythematosus of the face. Recovered in six months. Relapsed slightly for one week five months ago, and again early in September, 1925.

Lesion on back appeared twelve months ago and has never disappeared. Lesion on left thigh and left leg appeared seven months ago.

September 18, 1925.—Came to St. John's Hospital. He then had a widespread, rather diffuse lupus erythematosus on face, symmetrically arranged: atrophic patches in front of both ears and on each jaw: stippling visible in these places and on the nose: a patch on the left side of lower lip: a patch of very irregular outline and measuring about 3 in. in each direction on the lumbo-sacral region in the middle line: on the outer side of the lower thigh and inner side of the left leg an eruption made up of rings, $1\frac{1}{2}$ to 2 in. in diameter, and about $\frac{1}{4}$ in. wide, red and rather scaly, enclosing normal-looking skin. Irritation very slight.

Wassermann negative. Has improved rapidly and continuously on quinine sulphate 5 gr. by the mouth and lotio calaminæ locally, except as regards the lesion on the back, which appears to be unaltered.

Query.—Are the lesions on the back and thigh possibly lichen planus? A biopsy will be made.

Discussion.—Dr. G. PERNET considered that the lesions on the patient's back were lupus erythematosus. They were very similar to those in the middle of the back in a case shown by himself (Dr. Pernet) in 1923¹—that of a woman suffering from disseminated lupus erythematosus associated with Raynaud symptoms and early sclerodactylia.

¹ Pernet, G., *Brit. Journ. Derm.*, 1923, xxxv, pp. 335-6;

2 Dowling: *Schamberg's Disease*; Roxburgh: *Lichen Planus*

Dr. J. M. H. MACLEOD said he thought the lesions were those of lupus erythematosus, and he was not surprised at the difficulty of getting rid of them.

Dr. L. SAVATARD said he thought the lesions on the back were lichen planus, though the condition on the face was lupus erythematosus. A biopsy would settle the point.

Dr. S. E. DORE expressed his agreement with Dr. Roxburgh and Dr. MacLeod. Chronic patches of lupus erythematosus were not uncommonly seen on the trunk and limbs as well as in the more usual sites of distribution of the disease.

Dr. J. H. SEQUEIRA (President) said he thought the condition was lupus erythematosus. He said he had a very advanced case in his clinic, in a woman who had been attending there several years. She had most extensive scarring on the back, which was the result of undoubted lupus erythematosus of this type. He asked Dr. Roxburgh to bring up microscopical sections at a later meeting.

Case of Schamberg's Disease.

By G. B. DOWLING, M.D.

M., AGED 42, tailor. No history of trauma. This man attended my out-patient clinic on account of a patch of Schamberg's disease on the left forearm. He has had the condition for two years. It is quite typical in appearance and is of no interest except for the fact that it is limited to the left arm. In addition to the main patch, fresh patches are developing very gradually.

Histologically this case reminds me of a case exhibited by Dr. Roxburgh,¹ a thinned epidermis with flattened papillæ, and a rather dense subepidermal round-cell infiltration, tending to be aggregated in patches. No vascular changes observed.

Discussion.—Dr. A. M. H. GRAY said that occasionally Schamberg's disease was seen on the arm; he had shown a case four or five years ago, in which it was well marked on both arms.

Dr. SEQUEIRA (President) said it was interesting to have these cases shown, as there was a considerable belief that varicose veins were the underlying cause of Schamberg's disease. It was evident from the lesions on the arm that this hypothesis was incorrect.

Case of Lichen Planus Hypertrophicus.

By A. C. ROXBURGH, M.D.

G. F., MALE, aged 44.

1916.—Began to notice "pimples" at back of right knee. Irritation slight. Took little notice of them. They gradually increased in size, but he thinks they have been stationary for some years now.

1925.—He first showed me the lesions at St. Bartholomew's Hospital, on October 1. There is a roughly triangular area at the back of the right knee about 2 in. each way, covered with slightly mauve-coloured lumpy lesions raised $\frac{1}{4}$ to $\frac{1}{2}$ in. above the surface. The surface of the lumps shows some dilated follicles with horny plugs, and a few drops of clear fluid oozed from the lesions when first handled. Individual lesions measure from $\frac{1}{4}$ to $\frac{1}{2}$ in., some are confluent, and they are elastic to the touch.

In June, 1924, he acquired syphilis and had a secondary rash when he first came to St. Bartholomew's. He has had thorough treatment with "914" and bismuth, and his Wassermann and Sigma tests were negative June, 1925.

On October 2 I excised the uppermost and most prominent lesion for section, which is shown. It exhibits hyper- and para-keratosis, patchy granulositis, acanthosis,

¹ *Proceedings*, 1925, xviii (Sect. Derm.), p. 33.

great irregularity in the size and shape of the papillæ and interpapillary processes; in some places the basal layer is broken up and infiltrating cells are seen in the prickle-cell layer. There is an excess of pigment in the basal layer in the relatively normal skin at the ends of the section. In the subpapillary layer there is a massive infiltration of round cells with some plasma cells. In the cutis generally, which is much thickened, there are large numbers of capillaries with some cell infiltration around them.

At first I thought that the condition might be an example of "giant lichenification," described by Pautrier in *Annales de Dermatologie*, 1925, vi, p. 81, but, although the section rather resembles those illustrated in Pautrier's article, the gross lesion does not look much like his photographs, and I think it is an example of lichen planus hypertrophicus.

Discussion.—Dr. G. PERNET said that there was no doubt about this being lichen planus hypertrophicus, though it was in an unusual position.

Dr. J. M. H. MACLEOD said it was recognized that lichen planus might have its origin in a defect in the nervous system, and an interesting feature of this case was that itching, which was severe, was said by the patient to have been cured by his having undergone a biopsy, thus indicating a neurotic element in the case.

Case of Pityriasis Rubra Pilaris.

By A. WINKELRIED WILLIAMS, M.B.

PATIENT, aged 72, has recently had severe mental strain owing to loss of her husband and to financial stress.

First seen August 8, 1925. Lesions resembled lichen planus without typical planus papules but with outlying acuminate papules. Diagnosed as lichen planus and treated with carbolic acid and perchloride of mercury in zinc ointment and parathyroid internally. A week later fine-pointed papules on the backs of the fingers, visible only through a lens. No rash in mouth. On September 24 the patient was distinctly worse, and the ointment was causing considerable irritation. It was replaced by ol. cadini 20 minims, in 1 oz. of Lassar's paste. This caused greater discomfort. I altered my diagnosis to pityriasis rubra pilaris and prescribed an ointment of acid. salicylic., 4 gr. to the ounce. I have brought her up for further opinion.

Extensive Lupus Erythematosus with Miliary Papules.

By A. WINKELRIED WILLIAMS, M.B.

PATIENT, a friend of mine, about four years ago developed a typical discoid erythematosus lupus patch on scalp, and had very septic teeth. I advised him to undergo dental treatment. This advice was not taken for nearly four years, when I saw him again. The area had extended over the right side of the scalp, crossing the middle line in front, and the right side of the face was also severely involved. The eye was closed by oedema. The severe myopia was corrected. With the dioscope at this time minute pin-point-sized spots of ? apple-jelly tissue were seen. Two weeks ago the patches were covered with miliary nodules; in fact they have become converted into Leloir's lupus erythematosoides. Patient lives in the country and drinks a quantity of unboiled milk. The disease has not invaded fresh areas since the removal of the teeth.

Discussion.—Dr. PERNET said that years ago he saw a woman with severe lupus erythematosus of the face, and he noted that her teeth and gums were in a bad condition. He advised her to have her mouth seen to and the teeth extracted. Ultimately she had many teeth removed. He ordered calamine lotion only, and when he saw her a few months later, the lupus erythematosus had cleared up considerably.

Dr. J. H. STOWERS agreed with the diagnosis but regarded the case as a very unusual manifestation of the disease. Apart from local treatment he recommended the internal administration of large doses of quinine, which he had known to be of good service and which the late Dr. J. F. Payne originally proposed in the treatment of erythematous lupus.

Dr. WINKELRIED WILLIAMS (in reply) said that the treatment adopted had been soothing remedies, tincture of iodine and sun baths, and except for the removal of the teeth, he had not adopted any energetic treatment. He (Dr. Williams) said that during the coming winter the patient would be undergoing a course of carbon arc-light baths.

Case for Diagnosis (? Granuloma Annulare).

By M. SYDNEY THOMSON, M.D.

THIS patient, a girl, aged 3½ years, first attended the out-patient department of King's College Hospital on September 9, 1925. She was then suffering from three lesions, on the middle digit of the left hand (over the first interphalangeal joint), both insteps, the anterior aspect of the lower third of the left leg and on the left knee. Since that date they have all slightly increased in size. The mother states that the first patch to appear was that on the left leg. It began as a small area during January last. One month later those on the insteps became evident. The lesions of the knee and hand have only been present since July. There is no history of tuberculosis in the family, nor has this patient any physical signs which might be interpreted as giving rise to suspicions of such an infection. Her own doctor treated her for ringworm when the patches were first noticed. No biopsy has yet been performed.

Case of Blastomycetic Dermatitis (Gilchrist).

By G. B. DOWLING, M.D., and R. R. ELWORTHY, O.B.E., M.D.

PATIENT, a male, aged 22. At present under the care of one us (G.B.D.) as an out-patient at the West London Hospital.

Italian, but born and bred in Hammersmith. Wood-chopper by occupation.

History.—The primary lesion appeared about five months ago as a granulomatous infiltration of the nail-fold of the right index finger. There is no clear history of trauma. Further cutaneous lesions developed in the course of the ensuing two months, all upon the uncovered parts.

About two and a half months from the onset a swelling of the lower end of the left forearm appeared and slowly increased in size. This swelling was due primarily to bony enlargement but was followed in about a week by development of an abscess over it. This broke down almost immediately and discharged thin pus.

Further abscesses appeared at about the same time in other places, notably a large one about the size of a hen's egg in front of the manubrium sterni. They were not painful and broke down spontaneously within about a week. During the past few weeks the left knee-joint and the left ankle have become swollen; both have given rise to moderate pain.

Examination.—The patient is a man of rather poor physique, but he has a good colour and states that he feels quite well. General examination reveals nothing of importance. There are no physical signs in the lungs, cardiovascular system, or abdomen. The urine is normal. No pyrexia.

Cutaneous Lesions.—A granulomatous infiltration of the nail-fold of the right index finger, surmounted peripherally by a few small warty excrescences. About sixteen other cutaneous lesions at present situated upon the forehead, face, back of the neck, hands, wrists, and one on the left forearm. One of the largest lesions, measuring about 1½ in. by 1 in., is situated over the outer angle of the right orbit. It

is an indolent inflammatory tumour with a flattened surface, studded with warty projections, and a dark-red, raised, indurated border. By lateral pressure little beads of pus can be expressed between the papillomatous outgrowths, especially close to the border.

On the left side of the nose a similar, though rather smaller, lesion is present, involving the mucous membrane, as well as the skin; this, by spreading centrifugally, has partially destroyed the soft tissues overlying the cartilage.

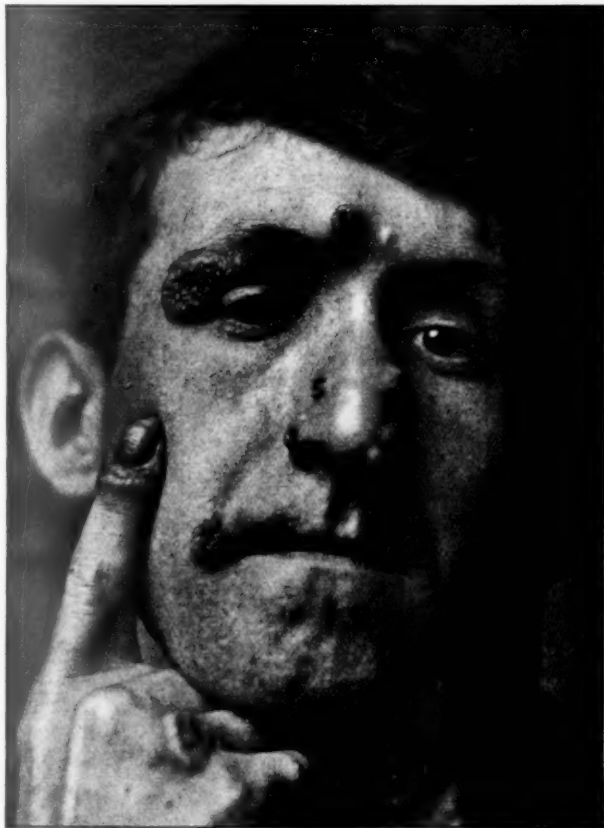


FIG. 1.—Dr. Dowling's case of blastomycetic dermatitis.

The remaining cutaneous lesions are of the same type but vary in size, the smallest being a pea-sized nodule with unbroken epidermis. The cutaneous lesions are practically painless.

Metastatic Subcutaneous Abscesses.—One has been present over the manubrium sterni but is replaced by a widely patent discharging sinus. Another abscess is present on the right side of the neck discharging thin pus through a small opening.

6 Dowling and Elworthy: *Blastomycetic Dermatitis* (Gilchrist)

Metastatic Bone and Joint Lesions.—There is bony enlargement of the lower ends of the left forearm. Swelling of the left knee-joint with considerable excess of free fluid in the joint. A moderately painful swelling of the left ankle.

RADIOGRAPHIC INVESTIGATIONS.

(1) *Radius.*—Two areas of clearly demarcated bone destruction at the lower end, with periosteal thickening. The newly proliferated periosteal bone has broken down in one place.

(2) *Tibia.*—Area of translucency at the lower end.

(3) *Chest.*—Negative.



FIG. 2.—Lower ends of radius and ulna of left arm.

PATHOLOGICAL INVESTIGATIONS (BY DR. ELWORTHY).

Laboratory findings to date.

Sample 1.—3.5 c.c. pus aspirated from an unbroken abscess over the left wrist-joint.

(1) Inoculated richly on to (a) two slopes of Sabouraud's medium; (b) two slopes of glucose peptone agar.

After four days at room temperature one of the Sabouraud cultures and one of the glucose peptone agar slopes were incubated at 37° C.

Results.—No growth at room temperature after twenty days on either medium kept at room temperature.

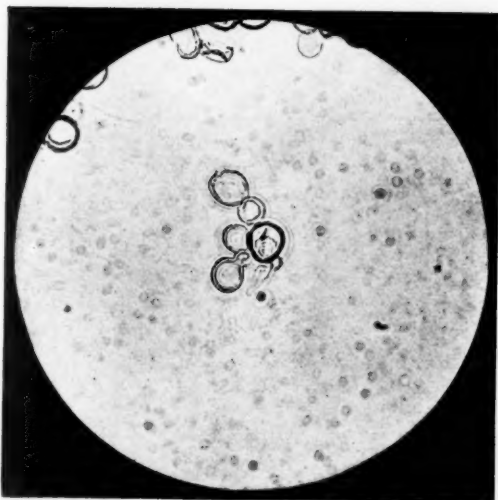


FIG. 3.—Three-day-old culture on trypsin blood-agar ($\times 500$).

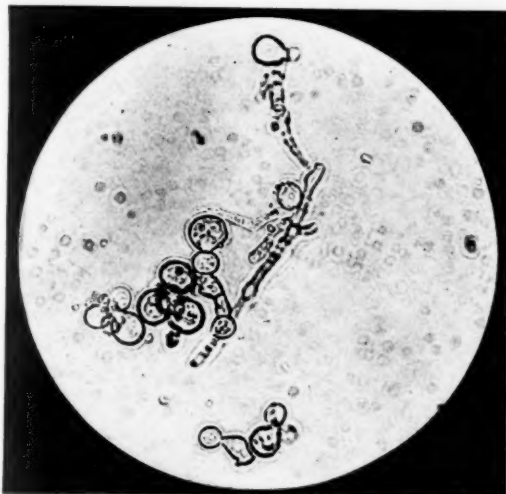


FIG. 4.—Three-day-old culture on "Lemco" blood-agar ($\times 500$).

8 Dowling and Elworthy: *Blastomycetic Dermatitis* (Gilchrist)



FIG. 5.—Early cutaneous lesion ($\times 25$).

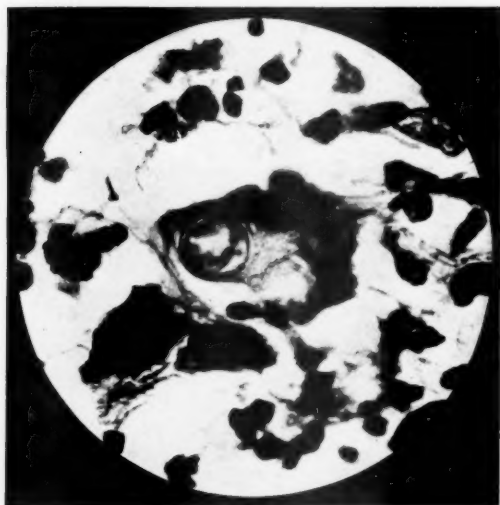


FIG. 6.—Tissue stage of organism in foreign body. Giant cell ($\times 1000$).

The glucose-agar slope on the fifth day at 37° C. showed commencing growth, whereas the Sabouraud still failed to do so.

(2) Sown thinly on :—(a) "lemco" human blood-agar (+ 0.75 Eyre) (incubated at 37° C.); (b) inspissated human serum.

After seventy-two hours, pin-point colonies were noted, which, on the following day, became very definite, round, cream-coloured colonies lightly poised on the surface of the medium, in places most thickly charged with pus. Three days after their first appearance on the blood-agar, the colonies became brownish, slightly rugose and convoluted. They are easily removed, and, though pasty in appearance, emulsify readily in saline.

With more prolonged incubation, and more particularly after repeated subculture, the organism tends to adhere to the surface of the medium and is more difficult to emulsify. But the growth does not submerge and so far has shown no inclination to adopt a true aerial habit.

The colour of the colony on serum and ordinary agar is nearly white and its appearance is somewhat featureless compared with those colonies on the blood-agar.

The budding form of the organism was difficult to demonstrate by direct methods in the pus, but in spite of this, many colonies occurred in the original cultures.

Apart from this fungus, other organisms could not be found in smears nor be grown in culture.

Sample 2.—Material consisting of pus and squamous epithelium expressed from a cutaneous lesion. Here the organism was easily found, occurring mainly in pairs, as shown, also in small groups consisting of three or four units. The organism varied in size, the commonest character of the single forms being 16 μ , of the budded 13 μ . An attempt at isolating the organism from this material failed, owing to the gross nature of the contaminations present.

A blood-culture was not successful.

A blood-count shows abnormal hæmoglobin and red-cell count. There is leucocytosis of 35,000, with polymorphonuclear neutrophils, 78 per cent.; eosinophils, 1 per cent.; basophils, 0.5 per cent.; hyalines, 0.5 per cent.; lymphocytes, 20 per cent. Specific agglutinins have not yet been proved to be present in the patient's serum.

Histologically, there is seen a papillary dermatitis possessing a granulomatous base and framework, rich in giant-cell formations, showing a prominent eosinophilia and a rich vascularity. True suppuration is a feature (caseation being absent). Small abscesses occur in the corium and inside the papillary downgrowths. Extravasated blood, exuded pus and exfoliated epidermal cells form a crust and lie in between the folds of corrugated epidermis. The latter is hypertrophied and distorted. It shows a diffuse infiltration with polymorphonuclears and focal areas, large and small, of invading granulomatous tissue and pus-cell accumulations.

The organism appears scantily as rounded cells with a thick cuticle, singly or in pairs :—(1) in the crust and interpapillary pus; (2) in the small abscesses in the corium; (3) within the abscesses occurring in the papillary downgrowths; (4) in giant cells. They have not yet been found in sweat- or sebaceous glands, in the unaltered or little altered epidermis, nor in the granulomatous tissue except at the places where small abscesses have formed.

Apart from the rarity of the disease in this country, the case is of interest in that systemic lesions involving bones have followed very closely upon the appearance of the cutaneous disease. Of the cases recorded in America up to 1914, only three cases of primary cutaneous blastomycosis had become generalized, and these only after an interval of from seven to twelve years.

It is curious that the wood that this man chops is obtained from the packing-cases in which cars are brought over from America to this country. I cannot help thinking,

however, that the original mould from which his infection has been derived may be growing in his dwelling, which is in a slum situated almost on the bank of the river at Hammersmith. Some pictures in Stober's paper¹ of the rotting floor boards of the hovels where some of the Chicago patients lived illustrated a luxuriant growth of a mould. This mould was found to differ in minute particulars only from human *Blastomyces*.

Discussion.—Dr. SEQUEIRA (President) said he had made the diagnosis of blastomycosis in a case many years ago, but, so far as he knew, this was the first case of systemic blastomycosis which had been seen in this country.

Dr. J. M. H. MACLEOD said it was a wonderful thing to see, in this country, a case of blastomycotic dermatitis of the systemic type. In his collection he had a good deal of tissue which was sent to him from San Francisco from a systemic case, and that tissue had the same appearances as the specimens shown by Dr. Dowling. This tissue showed the characteristic histology, it also exemplified the fact that the organism in the systemic cases multiplied by sporulation, and one of Dr. Dowling's specimens showed the endospores. He had specimens of the internal organs, all showing groups of those organisms, like the smaller ones shown in the culture demonstrated. So long as the yeast was reproduced by budding it did not do much harm, but the moment it began to reproduce itself by means of endospores, there resulted a collection of organisms smaller than red blood-cells, which readily passed through the vascular system, causing rapid and acute systemic infiltration.

Dr. L. SAVATARD said that in sections sent to him by Professor Gilchrist, Baltimore, of a systemic case of the disease the lungs showed a pure culture of the organism, and he wondered whether in the present case the sputum might show some evidence of lung involvement.

Case for Diagnosis (? Mycosis Fungoides).

By HALDIN D. DAVIS, M.B., B.Ch., F.R.C.S.

PATIENT, a well-preserved man, aged 72. Four years ago a patch of so-called "eczema" first appeared on the inside of the left shin. Since then this patch has grown considerably and now extends from the ankle to the knee, and, in addition, many other patches have appeared, both on the same leg and on the opposite one extending upwards to the groin (in which the glands are considerably enlarged). They have in several places become confluent. The patches are dry and the skin is infiltrated; between the lesions, which are sharply delineated, are islands of normal skin which have, mostly, circinate and geometrically shaped edges, a point of importance, I think, in arriving at a diagnosis. The original patch has now become considerably inflamed, since the patient rubbed some germolene into it, and in the middle of the patch there is a considerable heaping-up of tissue, almost approaching tumour formation. I have removed for microscopic examination a small piece from the edge of a lesion just above the knee. I do not think I ought to have taken it from the edge, as the changes are only beginning there, and are not so marked as they probably are in the central portions. The section shows great infiltration of cells in the corium, and signs of growing down and thickening of the interpapillary body. You will gather from what I have said that I think the diagnosis of the condition is mycosis fungoides. This conclusion is supported by the facts that the patient complains of great itching and that the patch which was heaped up in the middle has been much reduced by the small dose of X-rays I gave him ten days ago.

Dr. DOUGLAS HEATH agreed with Dr. Haldin Davis's diagnosis. An interesting feature was that no patches appeared in the upper part of the body. He had been watching a woman who had a similar eruption. She had had one tumour on the forehead, and he (the speaker) had regarded it as mycosis fungoides for eighteen months. It was treated by X-rays and the lesion disappeared. One or two other patches had come out since, and after application of X-rays they had also disappeared. He had seen many cases which had an eczematoid aspect, and they had remained quiescent without flaring up.

¹ Stober, *Arch. Int. Med.*, April, 1914.

Case of Mycosis Fungoides, (?) Leukæmia Cutis.

By J. A. DRAKE, M.D.

PATIENT, a male, aged 64, who, for more than a year, has suffered from a rather diffuse erythematous eruption all over the body, with scaling, and hyperkeratosis of feet and hands. When I first saw him, three months ago, the condition suggested an arsenical dermatitis, but there was no history of his having been brought into contact with arsenic, or of his having taken it, and no arsenic was found in the urine. Another tentative diagnosis was that it was a cutaneous manifestation of a leukæmic condition, and this supposition was fortified by finding that he had markedly enlarged lymphatic glands and that the blood showed a high leucocyte count, approximately 20,000 per c.mm., with a relative increase of lymphocytes. Later, however, one wondered whether it might not be a case of very early mycosis fungoides.

Discussion.—Dr. J. H. STOWERS confirmed the diagnosis of this case and referred to the usual, though variable, lesions in the premycotic stage in developing mycosis fungoides which he recognized as existing on the patient's body.

Dr. F. PARKES WEBER asked whether valuable diagnostic help could not be obtained by careful examination of the various types of cells in the infiltrated skin. The cellular infiltration of the skin in cases of mycosis fungoides was different from that in leukæmic cases. He inclined to the view that the present case was one of leukæmic nature, but a careful analytical examination of the relative proportion of the various types of cells in the infiltrated skin ought to settle the question.

Dr. DRAKE (in reply) said that sections of the skin of the case showed a well-marked carpet of cells beneath the epidermis, many of which were lymphocytes, but not all; there were a number of cells of the endothelial type. The gland seemed to show only chronic inflammatory changes. If this were mycosis fungoides, he thought it was rare to find, in this early stage, both enlarged glands and leucocytosis. But on looking through records he had been struck by the rare mention of any blood changes in mycosis fungoides. Possibly a case of this type showing blood changes might supply a link in the supposed connexion between leukæmia and mycosis fungoides.

Case of Granuloma Annulare with Subcutaneous Nodules.

By W. N. GOLDSCHMIDT, B.Ch.

PATIENT, girl, aged 3½, was admitted into Great Ormond Street Children's Hospital, under Dr. Thursfield, with the characteristic lesions of granuloma annulare on both feet. There was a five months' history of lumps under the skin, and at the date of admission there were several of these subcutaneous nodules on the legs and arms; they were movable in the deeper tissue and free from the skin. These have disappeared, except for one just below the right olecranon, and that nodule is very firmly fixed to the deeper tissue. The skin is not discoloured. The association of subcutaneous nodules with granuloma annulare seems to be very rare. A nodule like that now remaining was described by Dubreuilh, in one of the cases quoted by Dr. Graham Little in 1908.¹ A case was also shown by Dr. Gray in 1914, but those nodules were attached to the overlying skin. In 1923 a case was described by Ornstein in which the subcutaneous tissue was involved, and it was shown to be histologically the same as the cutaneous nodules. Injection into two guinea-pigs supplied no evidence of tuberculosis. Tuberculin tests in the case shown were all negative. The lesions began to clear up after excision for biopsy, a common occurrence even in parts not covered by the bandage. This reminds one of the behaviour of warts. This girl has no symptoms or signs of rheumatism and no history suggestive of such an infection.

¹ *Proceedings*, 1908, i (Sect. Derm.), pp. 99, 100.

12 Goldschmidt: *Granuloma*; O'Donovan: *Lupus Hypertrophicus*

Dr. A. M. H. GRAY said that when he showed his case some years ago¹ he was struck by its similarity to another case, which had not been shown, that of a child who had a large number of "rheumatic" nodules about the elbows, and associated with these, many infiltrated erythematous patches on the backs of the hands, which did not look like granuloma annulare, as they were not in the form of rings. They were infiltrated plaques, and were hyperkeratotic on the surface. He thought it was linked up with some of the curious persistent erythemata which were occasionally associated with these subcutaneous infiltrations, and it had been his view that granuloma annulare belonged to that group of case. The view held by some authors as to the relationship of granuloma annulare and cutaneous sarcoids did not seem to him a very satisfactory one.

Case of *Lupus Hypertrophicus*.

By W. J. O'DONOVAN, M.D.

A WELL-GROWN young man of 20 with a swollen, purple, nodular, infiltrated, ulcerated and scabbed face. This is a hideous deformity, but there is no present destruction of tissue. There is a similar area 5 in. in diameter on the site of the left nipple. The disease has been noticed for thirteen years and has been entirely neglected. Palate ulcerated. There is no apparent visceral disease. He has been sent for treatment by the county authorities. I am unable to give any prognosis. The treatment is to be slight baths in the first instance. Any progress made will be reported to the Section.

Dr. SEQUEIRA (President) said he had had a case of similar type. In spite of all treatment, the disease spread relentlessly and the patient died from carcinoma.

¹ *Proceedings*, 1914, vii (Sect. Derm.), p. 163.

Section of Dermatology.

President—Dr. J. H. SEQUEIRA.

Case of Lichen Planus of the Scalp.

By ARTHUR WHITFIELD, M.D.

I HAVE brought this patient because I think perhaps the lesion of lichen planus on the scalp is not very well recognized; I believe that it occurs more commonly than is generally supposed.

This patient came to the hospital about a month ago with a history of scalp trouble existing from six to eight months. At that time there was a raised, sharply-delineated, red disc about one and a half inch in diameter above the left ear on the hairy scalp. The patient had been applying ointment and the surface was free from scales, but there were small, funnel-shaped enlargements of the apertures of the hair follicles. There was also an infiltrated papule on the glabrous skin just below the side hair.

I diagnosed lichen planus of the scalp, and on inquiry found that the patient had "some spots on the stomach," which proved on examination to be typical lichen planus, thus corroborating the diagnosis of the scalp.

The view I wish to submit to you is that lichen planus of the scalp can be diagnosed accurately from its characteristics provided that sufficient attention is paid to the corroboration when possible, as in the present case, by the usual lesions elsewhere.

The points to which I would draw attention are the following: (1) The lesion is always sharply defined and nearly circular; infiltration is marked so that a kind of "tableland" is produced. (2) The hair may be broken from rubbing or somewhat distorted by the abnormal keratosis. (3) If no treatment has been used the surface of the lesion is covered with small silvery scales which are somewhat adherent, and if these are stained no organisms are found in them; if ointment has been rubbed in, the scales are absent, and the funnel-shaped depressions already alluded to are seen. I have left this patient without local treatment and the patch now shows the scales. There is no atrophy present, and there are no follicular lesions with spines.

Discussion.—Dr. GRAHAM LITTLE said that the case was exactly like that of a patient whom he (the speaker) had shown at a recent meeting. In that case there had been typical lichen planus of the scrotum and penis and patches of atrophied baldness on the scalp, with exactly the same arrangement of follicular plugs around the atrophied patch that Dr. Whitfield had described in the present case. He (the speaker) was particularly interested in this type of lichen planus, and he now believed that certain cases which he had described some years ago as "folliculitis decalvans atrophians" were really cases of lichen planus. Those cases had been accompanied by follicular eruptions upon the smooth skin (indistinguishable from lichen spinulosus) as well as by atrophic scarring of the scalp. But since that observation certain intermediary cases had occurred which in his (Dr. Graham Little's) opinion served to link up the earlier cases with lichen planus.

14 Roxburgh: ? *Lupus Erythematosus*; *Cutis Verticis Gyrata*

Section from Case for Diagnosis (? *Lupus Erythematosus*),
shown October 15, 1925.¹

By A. C. ROXBURGH, M.D.

I SHOWED a case at the last meeting and the question to be decided was whether the condition was lupus erythematosus affecting the back, or whether it was lichen planus. I am now showing a section, but I do not think it throws much light on the subject; it is not typical of either condition.

Discussion.—Dr. WHITFIELD said that he thought the section established the diagnosis of lupus erythematosus. On looking at the central part of the section one found that all the papillae were flattened out, so that the epidermo-papillary junction was a straight line; there was no subepidermic lacuna; there was an oedematous rarefaction of the pars papillaris with a row of fibroblasts having their long axes horizontally placed, like a row of soldiers lying down. These were in his (the speaker's) opinion the characteristics of lupus erythematosus.

Dr. MACLEOD said he concluded from the section that the case shown by Dr. Roxburgh last time was not one of lupus erythematosus, and he did not consider that in the section now shown there was sufficient rarefaction of the fibres in the papillary body to warrant the diagnosis of that disease.

Dr. J. H. SEQUEIRA (President) said that from an inspection of the section he agreed with Dr. Whitfield.

Case of *Cutis Verticis Gyrata*.

By A. C. ROXBURGH, M.D.

THIS patient, a male, aged 25, a Jew born in London of Polish parents, was shown at a meeting of the Section by the late Dr. Maurice G. Hannay, in March, 1923,² and at that time he had noticed the scalp condition for nine months only. It has altered very little since then. The scalp is thickened and thrown into folds suggesting the gyri and sulci of the cerebral hemispheres. The hair has fallen partly or completely on the summits of the ridges, but persists in the sulci. Dr. Hannay had described the skin of the trunk and limbs as exhibiting a chronic dry pruriginous condition which had existed since childhood; it was, in fact, because of this irritation that the patient had come for treatment, not for the condition of his scalp. When I saw him a month ago the skin of his body was dry: on parts of the trunk there was a kind of permanent goose-skin appearance suggesting pityriasis rubra pilaris, and there were large erythematous scaly patches on the upper parts of the arms, neck and chest. There are no definite lesions of pityriasis rubra pilaris on the phalanges, however, nor is the skin of the palms and soles thickened, and I should like to know whether the members of the Section consider that the condition of the skin could be regarded as pityriasis rubra pilaris or not.

The first case of cutis verticis gyrata was described by Jadassohn, and others have been described since, notably by Unna. There are two theories as to its nature, one that it is a result of some form of chronic inflammation and the other that it is due to the slow development of a congenital abnormality. Histologically, Dr. Hannay's section showed a mild degree of simple inflammatory reaction chiefly about the hair follicles; and in a case in Italy, that had been examined post mortem, and was described by B. Sparacio in the *Riforma Med.*, April 14, 1924, the scalp was loosely attached to the periosteum and there was a slight perivascular infiltration in the papillary layer.

All the cases so far described, according to Stelwagon, have been in males, and all, except one, in dark-haired persons.

Dr. A. WHITFIELD said that he did not regard the case as pityriasis rubra pilaris; he thought these juicy papules were part of a general toxic dermatitis.

¹ *Proceedings*, 1925, xix (Sect. Derm.), p. 1.

² See *Proceedings*, 1923, xvi (Sect. Derm.), p. 88.

Case of Pityriasis Rubra Pilaris.

By A. C. ROXBURGH, M.D.

R. H., MALE, aged 22, attended King's College Hospital under Dr. Whitfield seven years ago, when he had only a few lesions on the elbows, hands and feet. I understand that Dr. Whitfield then made a tentative diagnosis of pityriasis rubra pilaris. Four months ago the condition became much worse, and the arms, back, scrotum, and thighs became affected. When I first saw him at St. John's Hospital on October 6, 1925, he had the typical horny papules of pityriasis rubra pilaris on the backs of the hands, fingers, and elsewhere, much thickened skin on palms and soles, and large sheets of erythematous, slightly scaly skin symmetrically disposed on backs and outer sides of the arms, on each side of the chest and over the whole of the back of the trunk and thighs from the scapulæ to knees. Over the sacral region the skin had characteristic "nutmeg-grater" feel. The scalp and face are but little affected and only a few of the toe-nails exhibit hypertrophy. The patient has improved during the last month, but I should be glad of any suggestions for treatment.

Discussion.—Dr. WHITFIELD said he remembered this case as he had seen it seven years ago. At first it had caused him considerable difficulty, because the only complaint then had been that of a hyperkeratotic condition of palms and soles, and there had not been any trace of an initial lesion. There had been a curious long, spindle-shaped area on elbows and knees, of a very peculiar coral pink colour, also a scaliness; there were none of the spines of pityriasis rubra pilaris; the scales were chalky and could be picked off, causing a very sandy feeling between the fingers.

With regard to treatment, he (the speaker) had had a patient who eventually grew out of this disease without much help from internal treatment, though he improved with sea-bathing. This bathing was substituted, when the patient came home, by his taking baths of 3½ per cent. salt solution, alternating with potassium sulphide. No internal remedies seemed to have any effect at all. Especially he would add that the administration of raw sheep's thyroid pushed to the extreme limits of tolerance had no effect at all.

Dr. KNOWSLEY SIBLEY said that in 1913 he had shown before the Section the case of a small boy who had very severe pityriasis and who had been in St. John's Hospital with severe illness and a high temperature.¹ There had been furrows in the scalp into which the finger could be placed. The condition had however cleared up in a few weeks, and the boy had gone home well. A few months later, typical guttate psoriasis had developed over the greater part of his body.

Dr. J. H. SEQUEIRA (President) said that the relationship of this condition to psoriasis had interested him very much; he had seen cases which had been diagnosed as psoriasis and pityriasis rubra pilaris alternatively. He (the speaker) believed that Dr. Adamson thought pityriasis was a follicular type of psoriasis.

Dr. H. G. ADAMSON said that he would not give it as his definite opinion that pityriasis rubra pilaris and psoriasis were one disease, but he was inclined to take that view. Some years ago (*Brit. Journ. Derm.*, 1911, xxii, p. 181), he had shown a case of typical pityriasis rubra pilaris, in which the patient recovered after an attack of measles, and a few months later had an attack of typical psoriasis on the elbows and knees; that was not the only case of the kind he (Dr. Adamson) had seen. Again, it was not uncommon for other members of the family to suffer from psoriasis (see also *Brit. Journ. Derm.*, 1912, xxiv, p. 280, and 1913, xxv, p. 238).

Case of Lupus Vulgaris et Erythematosus.

By W. KNOWSLEY SIBLEY, M.D.

A. J., FEMALE, aged 37, married. At the age of 16 enlarged glands were removed from her neck on the right side, and when she was 23, more glands were excised from the supraclavicular region. At 24 years of age she first noticed a small patch

¹ See *Proceedings*, 1922-23, vi (Sect. Derm.), p. 161.

of lupus on her right cheek. A sister, aged 26, had had a patch of lupus on her nose for two years, and died in 1919 from phthisis and tuberculous peritonitis.

She came under my observation in February, 1917; there was a patch of active lupus on the right cheek $1\frac{3}{4}$ in. and on the right side of her nose $1\frac{1}{2}$ in. The latter patch had been there nine months. There were enlarged glands in the right sterno-clavicular region. She had also a mitral systolic murmur.

Up to that time she had been treated with X-rays and also with applications of acetone CO_2 . Since then she has been treated with ionization (zinc sulphate) and X-rays. She had also received applications, in painting, of trichloroacetic acid and acid nitrate of mercury. For the last six months she had been treated with ultra-violet rays.

There is now a considerable amount of depression and scarring over more or less the whole of her right face, but the lupus appears to be quiescent. There are some four more or less circular patches of lupus erythematosus on the scalp, with complete alopecia. These, together with the patch in front of the right ear, were first noticed about three years ago.

Discussion.—Dr. WHITFIELD said he saw this case in 1913, and he believed that at that date he diagnosed the face condition as lupus erythematosus; the patient had then no lesion of the scalp. He (Dr. Whitfield) believed his view at that time was, that it was an infiltrative type of lupus erythematosus. He would, if necessary, produce the notes.¹

Dr. J. M. H. MACLEOD agreed with Dr. Whitfield's opinion concerning the case; he considered that lupus erythematosus was enough to account for all the atrophy seen. He did not remember having seen lupus erythematosus and lupus vulgaris on the same face at the same time.

Dr. J. H. SEQUEIRA (President) agreed that at times it was difficult to make a diagnosis between the two conditions, but he did not remember having seen an actual association of the two diseases in one patient. And he would emphasize a point which had been raised by Dr. MacLeod, that occasionally there were cases of lupus erythematosus which caused very considerable atrophy. He had in mind a case in which hemiatrophia facialis was associated with lupus erythematosus.

Sections from a Case of Myeloma.

Shown by J. M. H. MACLEOD, M.D., and A. PINEY, M.D.

THE patient, a woman, aged 35, came to Charing Cross Hospital with a peculiar, slightly raised, blue-black, pigmented patch, circular in outline, about three-quarters of an inch in diameter, and situated on the posterior fold of the left axilla. It had been in existence for two years, and there was no history of any previous lesion, such as a mole. The axillary glands were not enlarged. The appearances suggested a melanotic carcinoma, and it was thought advisable to have it freely excised.

On microscopical examination it appeared to be a myeloma, a type of tumour which must be very rare in the skin, as we were unable to find any reference to it in the literature. The most striking feature in the histology was the presence of a large amount of pigment, which was not melanin, as was expected, but hæmosiderin, and which gave a Prussian-blue reaction with potassium ferrocyanide and hydrochloric acid. The ground substance of the tumour was composed of loose, active-looking fibrous tissue, in which were a number of newly-formed vessels, with apparently incomplete walls. There were a very large number of giant cells embedded in the fibrous ground substances. These were extremely large cells, with many nuclei in each, but there was no sign of nuclear activity, or of cell division. Where the

¹ Note.—On subsequently looking up the notes, it was found that the patient in 1913 presented typical lesions of lupus erythematosus of the face and no sign of lupus vulgaris.—A.W.

pigment was most plentiful, there was well-marked cellular degeneration, which, in places, had resulted in formation of small cysts, partly filled with pigment, some intracellular, some extracellular.

The giant cells were similar to the osteoclasts of myeloid sarcomata connected with bone. The complete absence of fat from the tumour seemed to show that it differed from a xanthomyeloma of a tendon sheath.

Dr. F. PARKES WEBER said that an examination of the sections of the tumour showed (besides sarcoma-like cells) two very striking classes of cells: (1) Phagocytic cells, the cytoplasm of which was loaded with large granules of pigment (hæmosiderin), evidently derived from the abundantly effused blood in the tumour. These phagocytic cells, crammed with hæmosiderin, were doubtless of the nature of macrophages (Metchnikoff) or histiocytes (Aschoff), and were very numerous in some parts of the sections; there were spaces apparently once filled with blood in which they were specially numerous. (2) Multi-nuclear giant-cells, probably allied to foreign-body giant-cells, the representatives of which in the healthy body were the osteoclasts. The Langhans giant-cells of tuberculous lesions were only a variety of foreign-body giant-cells, and similar foreign-body giant-cells occurred in abundance in tumours of the xantho-myeloma class ("myeloma of tendon-sheaths," &c.). The chief feature of the sections was, however, the enormous number of the phagocytic cells (histiocytes) mentioned above. Were these present merely as scavengers, owing to the effused blood, or were they themselves tumour-cells? In other words, was the tumour derived from the normal histiocytes of the body, or rather from mother-cells of the histiocytes ("histioblasts")? Some tumours probably really were derived from the normal histiocytes or histioblasts of the body. Possibly tumours of the xantho-myeloma class were derived from them. Recently Harvey Cushing (Cameron Lectures, Edinburgh, October, 1925) claimed that meningiomas (so-called "endotheliomas of the dura mater") were derived from the meningocytes, which were histiocyte-like cells, like the Kupffer cells of the liver and other phagocytic cells of the reticulo-endothelial system.

Case of Multiple Superficial Rodent Ulcers.

By H. MACCORMAC, C.B.E., M.D.

THE patient, a woman aged 74, first showed "spots on the skin" some five years ago. She now presents three well-marked rodent ulcers of the superficial type to which Dr. Graham Little has devoted particular attention. The two lesions situated on the back are of the usual characteristic form. The third, seen on the left thigh, a relatively large lesion with a distinct rolled edge, is unusual in that a small growth of the cystic type the size of a pea appears on the surface. This combination of two distinct and uncommon varieties of neoplasm is, in the exhibitor's experience, rare.

Discussion.—Dr. GRAHAM LITTLE said he had had a case very much like this, one of the first cases of the type to be demonstrated. There was a large flat, rodent patch on the back (erythematoid benign epithelioma type) with a cystic rodent developing on it, and it persisted, without any malignancy, for nineteen years. Then the patient came up again, and the rodent ulcer had a much more malignant appearance. The whole of the ulcer was ultimately excised by Mr. Warren Low last year. The histology of the late development showed typical malignant squamous-celled carcinoma. The sections taken in 1906 showed cystic rodent ulcer, so a definite change had taken place in the histology of the lesion between 1906 and last year.

Dr. WILFRID FOX said that the late Mr. Clinton Dent had a case of the kind in which he (Mr. Dent) had excised the ulcer five years previously. At the time that he (the speaker) was acting as house-surgeon to him, Mr. Dent excised it again, and its nature was the same, namely, cystic rodent. Ten years later a recurrent growth was excised by another surgeon, and then it was typical epithelioma. The same pathologist examined all three specimens, so the personal equation could be excluded. It was not of the Hutchinsonian crateriform ulcer type.

Dr. J. H. SEQUEIRA (President) said this transformation from the basal to the squamous-celled type was a process to which Dr. MacCormac had called particular attention. He agreed that such cases were very rare.

Dr. MACCORMAC (in reply) said he was very much interested in the observations of the President, Dr. Wilfrid Fox, and Dr. Graham Little, because they supported the view he had advanced, that the so-called basal and prickle-cell types of cutaneous carcinoma were mere variants of the same process and not distinct forms of new growth. Indeed it was sometimes possible to observe the two forms of growth present in a single section, with the transition stages of the one form of cell into the other.

Case of Pigmentary Nævi.

By J. A. DRAKE, M.D.

THE patient is a girl aged 5, with multiple pigmentary nævi. These are present on both sides of the body, some being smooth, others warty. Many are "streaked," and one or two end abruptly at the mid-line of the body in front. There is a well-marked anal "dimple" at the upper part of the gluteal fold.

Discussion.—Dr. J. H. SEQUEIRA (President) asked Dr. Drake whether he would distinguish this condition from ichthyosis hystrix. He (the speaker) looked upon the latter as a variety of nævus. He asked for suggestions as to what should be done for these cases when they occupied a situation in which they caused disfigurement and the patient wished to have them removed. In his own experience scraping had been useless, as recurrence ensued. It was also unwise to attempt destruction by radium or X-rays. Where he had had the opportunity he had caused them to be excised, and grafts applied to the area.

Dr. H. SEMON said that his experience agreed with that of the President. Three months ago he treated a similar type of nævus which was situated on the back of the scalp in the case of a girl, by means of diathermy, and it took more than six weeks to heal; this indicated how deeply the treatment was carried. Later, however, the nævus began to grow again. He thought that nothing short of excision, and subsequent plastic repair, would be effective in this type of nævus.

Case of Parapsoriasis.

By E. G. GRAHAM LITTLE, M.D.

I SAW this patient, a man aged 47, on October 20, when he had a very extensive eruption upon the chest, back, front and limbs, consisting of sharply outlined red and faintly scaly patches showing some lividity and brown colouring in the larger patches, with a tendency for the patch to break up into follicular lesions. The patches show no induration and are moderately itchy. There are no glandular enlargements anywhere noticeable. The skin of the scrotum is red and rugose, and is considerably thickened; the itching is here most uncomfortable.

I regard the case as one of probable parapsoriasis, with an alternative diagnosis of a seborrhœid. During the months which have elapsed since I saw the patient he has been treated with practically nothing else but sedative baths, and the congestion of the patches has very greatly diminished, but they are still obviously present. I consider that there is too little infiltration to suggest mycosis fungoides.

Discussion.—Dr. J. A. DRAKE thought it would be of interest to have a blood-count done, in view of the possibility of a leukæmic condition.

Dr. J. H. SEQUEIRA (President) said that although there was not much infiltration the diagnosis of mycosis fungoides was not altogether excluded.

Dr. GRAHAM LITTLE (in reply) said that he found it difficult to distinguish early cases of mycosis fungoides from parapsoriasis.

Case for Diagnosis.

By E. G. GRAHAM LITTLE, M.D.

THIS patient, a man aged 36, a marine surveyor, has travelled extensively in most parts of the world. Nothing abnormal was detected until August, 1925, when the scrotum began to swell and, later, the penis also. There was no urethral discharge preceding the swelling and no pain at any time. Micturition is somewhat uncomfortable, but quite normally performed. Although the swelling began in the scrotum it has become much more accentuated on the penis, which, throughout its extent, has swollen to twice its natural size, and there is a hard œdema of the whole subcutaneous tissue. The swelling is temporarily reduced by hot fomentations, but not to any great degree. The testes are apparently normal; there are no glands enlarged, and the urine is entirely normal. No history of any venereal disease, and the patient is otherwise in good general health. No evening or other rise of temperature has been noted during three weeks spent in hospital.

Blood-films examined on three successive nights for *Filaria* showed no parasites, but there was some eosinophilia. Stools examined for bacteria showed nothing abnormal, and very few streptococci.

The acute onset, which took place while the patient was resident in England, appears to me to make the diagnosis of filariasis improbable. The patient has received two or three injections of a mixed staphylococcic and streptococcic vaccine (antisepsis vaccine, St. Mary's Hospital), but without very marked improvement.

Dr. A. CASTELLANI said he regarded the case as a very interesting one. He had seen similar cases in the tropics, especially in Ceylon. If he had seen this case in a tropical country he would have said it was probably incipient elephantiasis. In his experience, one or even several negative examinations of the blood did not necessarily exclude filariasis. The presence of eosinophilia was rather in favour of filariasis.

Case of Pityriasis Rubra Pilaris.

Shown by W. N. GOLDSCHMIDT, B.Ch. (for A. M. H. GRAY,
C.B.E., M.D.).

PATIENT, a farmer, aged 20. Six years ago his present disease began with a patch on the right shoulder, which spread rapidly all over the body. For the last three years there has been no considerable change. There is no tuberculosis in his family. But, as some authorities, including Dr. Adamson, think there is some relationship between pityriasis rubra pilaris and psoriasis, it is of some interest to learn that his aunt suffered from psoriasis. He now presents a typical picture of the disease. The skin is erythematous and very rough and harsh to the touch. The hair-follicles contain hyperkeratotic plugs. On the chest, back and scalp there is fine scaling. There are a few discoid patches on the leg which closely resemble psoriasis. The toe-nails are severely involved; the finger-nails less so. His subjective symptoms are the characteristic ones of tension. A von Pirquet test performed in the usual way with a scarifier proved negative. A second test carried out by pricking through the drop of tuberculin with a needle proved positive. As regards treatment, the patient says that some years ago, when he was under Dr. Beattie, arsenic was of assistance for a time. We have tried thyroid and salicylates but without success. I was interested in hearing what Dr. Whitfield and Dr. Barber had to say on this question.

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Section of Dermatology.

President—Dr. J. H. SEQUEIRA.

Multiple Recurring Ulceration of the Legs in a Young Woman.

By WINKELRIED WILLIAMS.

WHEN I first saw this girl, aged 17, in the summer, the backs of her legs were covered by ulcers, which looked like Bazin's disease. Wassermann negative. Later I applied 5 per cent. tuberculin (human) ointment to the ulcers, and kept it on for five days, and there was no reaction. Provocative injections were given in order to ascertain whether there was any inherited syphilis, but the result was negative, and the treatment did not bring out the Wassermann. I found that the early lesion was a little cyst in the corium, with practically no inflammation of the skin above. Puncture produced a clear fluid. Culture of this was sterile, including three weeks' incubation in proof-agar. There is no information as to hereditary syphilis, and there are no stigmata. Some Members have thought it might be artefact, but that is not my opinion. The treatment which brought about healing was parathyroid and locally a weak iodide of starch paste. Then the treatment was stopped, and in a few weeks she came with a recurrence. The condition has now been going on for years.

? Case of Multiple Idiopathic Sarcoma (Kaposi)

By H. C. SEMON, M.D.

THIS man, aged 64, was sent to me by Dr. Girling at the beginning of November. He was born of German parents at Elberfeld. He gave a history of severe pains in the legs for several years. The eruption on the fronts of the ankles, lower legs, knees, elbows, and recently on the penis, first appeared ten months ago. There is no itching, but some tenderness on firm pressure.

The pains in the legs and some other vague symptoms of which he complained were thought to be due to tabes. The blood Wassermann reaction was negative, but Dr. Reynell found it strongly positive in the cerebro-spinal fluid and confirmed our suspicions. In March of this year he had some difficulty in swallowing, with nasal discharge, and Mr. Gay French has kindly informed me that he made a diagnosis of gumma of the pharynx which rapidly cleared up under pot. iod. 30 gr. t.d.s.

There appear to be two types of cutaneous lesion: (1) tumours; (2) soft infiltration, which seems to precede the former, and in any case is localized to the same areas. The tumours vary in size from that of a pea to that of a pigeon's egg, and are bluish to brick-red in colour. There is no definite pigmentation, although some of them, e.g., on the forearm, show a hæmorrhagic tendency. They are definitely subcutaneous in origin, and in one case appear to be intramuscular (left forearm, extensor aspect) in position. They are disposed with almost accurate symmetry on the fronts of the ankles, the lower shins, the lower parts of the forearms and backs of the hands, while the localization on knees and elbows is that of psoriasis.

A soft infiltration of the left half of the glans penis appears to be on the point of undergoing tumour transformation. The tumours are in some cases, e.g., on the elbows and forearms, very tense, elastic, and hemispherical in shape, and in these the tendency to hæmorrhage is most pronounced.

The liver is enlarged three-fingers' breadth below the costal margin. A small nodule was excised from the left forearm and examined by Dr. Ellison, Assistant Pathologist, Royal Northern Hospital, by various staining methods. He states:—

"The blood-count is normal and serves to exclude leukemia. The urine contained no albumin or albumoses. Sections of the tumour show a somewhat thinned epidermis and a cellular mass in the cutis vera. . . . The cells of the mass present rounded ovoid and somewhat elongated nuclei, which stain rather lightly. Mitotic figures are present. Delicate intercellular processes surround individual cells. The endothelium of the capillaries is normal. Some of the larger vessels are thickened. Only one small hemorrhage has been found. There is no golden-brown pigment, and the test for iron was negative.

Hair follicles, sweat glands and ducts, fibrous tissue and unstriated muscle fibres are preserved intact in the midst of an actively growing cellular mass. . . . The condition suggests a chronic inflammatory process rather than a true neoplasm."

A tumour in the neighbourhood of the left olecranon process received a pastille dose of X-rays about a fortnight ago, and it now shows a definite decrease in size.

The diagnosis of Kaposi's idiopathic (so-called) sarcoma is offered—in spite of the absence of pigment—on the patient's origin (German-Polish), age, and probable Jewish extraction; on the history (as in Kaposi's original description) of a first appearance on the feet; on the symmetry and localization; and finally on the histology, which except for the absence of pigment coincides very closely with that reported by Kaposi, and more recently by Dr. Bulloch in one of Dr. Sequeira's cases.

Discussion.—Dr. PERNET said he considered that clinically the case came into the category of mycosis fungoides à tumeurs d'emblée. It reminded him of a case in a woman he had recorded in 1913.¹ The patient eventually was kindly taken into the Middlesex Hospital by the late Dr. Pringle, and came under the care of Dr. MacCormac. He (Dr. Pernet) understood from Dr. Semon that growths in his case were present before iodide of potassium was given.

Dr. F. PARKES WEBER said that the tumours in this case had a curious distribution for Kaposi's multiple idiopathic hæmorrhagic so-called sarcoma, especially the intramuscular tumour in the left upper extremity. He thought that the case might be one of mycosis fungoides commencing with tumours, as suggested by Dr. Pernet. He wondered whether the iodide given could have had any effect on the eruption. Could it be a granulomatous condition which had been influenced, first, by the old syphilitic condition of the vessels, and secondly, by iodide of potassium? He would like to know what was the effect of discontinuing the latter, and treating the patient with arsenic, and Roentgen rays.²

Dr. S. E. DORE said he did not consider this condition was mycosis fungoides, though some of the lesions resembled those seen in that disease. He had never seen such intensely hard, dome-shaped tumours, lasting for periods up to six months without breaking down in mycosis. The mycosis fungoides tumour was much softer and its centre broke down rapidly, so that it became flat or crateriform in shape. He regarded the case as probably one of multiple cutaneous sarcoma of the "Perrin" type.

Dr. H. MACCORMAC said he remembered the case to which Dr. Pernet referred, as the patient was under his care in the Middlesex Hospital, and eventually died there. The tumours were of a distinctly soft character, and many of them broke down, forming areas of ulceration. All the lesions were not in the skin, for the post-mortem notes recorded a tumour formation, lobulated in outline, of a pale brown colour, in places undergoing softening, lying upon the muscles of the thigh. In his view the case exhibited by Dr. Semon presented many similar features, and he was inclined to regard it as mycosis fungoides à tumeurs d'emblée. He suggested staining portions of the tumour for Altmann's granules, which were absent in sarcoma, but had been found by the speaker to be present in abundance in cases of mycosis fungoides.

Dr. J. H. SEQUEIRA (President) said he had seen most of the cases of multiple idiopathic pigment sarcoma in this country in the last twenty years, but he could not remember one in

¹ Pernet: "A case of mycosis fungoides à tumeurs d'emblée, unsuccessfully treated by salvarsan and X-rays." *Trans. Seventeenth International Congress of Medicine*, 1913, Section xiii, p. 189.

² By the kindness of Dr. Semon, Dr. Weber has had the opportunity of examining microscopic sections from the case with a pathologist, Dr. E. Bock. He suggests that, as the structure of the tumours is definitely one of small round cell sarcoma, the case might be regarded as one of true sarcoma, which by its purple colour, more or less symmetrical distribution on the lower extremities, and involvement of the penis, imitates some of the characteristics of Kaposi's multiple idiopathic hæmorrhagic so-called "sarcoma."

which there was the distribution which was a feature of the present case. In every instance the disease had begun at the periphery with pigmentary staining, and that staining and the oedematous thickening of the skin had always preceded the development of tumours. At first the tumours were of moderate size. The diagnosis in this case appeared to rest between *mycosis fungoides à tumeurs d'emblée* and sarcoma. Owing to the hardness of the tumours he inclined towards a diagnosis of sarcoma. It would be interesting to learn of the further progress of the case, and of the result of the test which Dr. MacCormac had suggested.

Dr. SEMON (in reply) said that under one dose of X-rays one of the tumours had partially involuted. The patient had 30 gr. of iodide of potassium three times a day under Mr. Gay French, in June, but was taking none now. There was a very definite enlargement of the liver, and that might suggest that there were secondary deposits in it already. He would have the suggested test carried out.

Postscript.—December 23, 1925.—Since the case was shown on December 17 the involution of the tumours in front of the ankles and on the left elbow region (which were treated by X-rays about December 10) had been very marked. It is only in *mycosis fungoides* that I have seen anything like it. A further point in favour of this diagnosis, which was suggested by Dr. Pernet, is the sudden appearance of symmetrical soft infiltrations in the skin of the forehead.—H. S.

Severe Atrophy following Lupus Erythematosus.

By J. M. H. MACLEOD, M.D.

PATIENT, a middle-aged woman, who has suffered for over twenty years from lupus erythematosus of the face. She has tuberculous glands, and there is a family history of tuberculosis.

The chief feature of the case consists in the lupus erythematosus having been succeeded by atrophy, which is steadily progressive, and produces an appearance simulating hemiatrophy of the face.

Case of Lupus Erythematosus.

By H. MACCORMAC, C.B.E., M.D.

PATIENT, a male, aged 42.

History.—Previous health good, except for the presence of a stricture, treated in 1916. The eruption for which he is exhibited began on the forehead five years ago in the form of a small red patch, attributed to sunburn. This patch gradually increased in size, and when the patient came under observation, two years ago, it had extended so as to cover the right brow. The condition was then of the nature of an erythema with telangiectases. There had been a gradual and progressive spread across the forehead and downwards over the right eye, with oedematous swelling of the loose tissue in the neighbourhood of the eye. Some slight degree of atrophy is present in the older part of the eruption. Local treatment with ultra-violet light, given three times a week for the last month, appears to have arrested the condition, and to some extent to have diminished it.

Dr. J. A. DRAKE said that one feature against the diagnosis of lupus erythematosus was the fact that the follicles on the forehead were intact; there was not the condition of atrophy of the follicles which one would expect in lupus erythematosus.

Case of Schamberg's Disease.

By H. MACCORMAC, C.B.E., M.D.

PATIENT, a girl, aged 14, first noticed a small patch on the left upper arm six months ago; other similar patches soon made their appearance on the left thigh, the flexures of the arm, neck, and groins. The eruption is now very widely distributed over the body in a symmetrical fashion, and is represented by areas of

various sizes and contour, of a brownish colour, upon which there appear numerous small puncta resembling grains of cayenne pepper. The condition would seem to correspond to the progressive pigmentary dermatosis first described by Schamberg in 1901. Schamberg, in his account of the disease, states that the patches are irregular in shape, non-elevated, of a reddish brown or burnt-sienna colour, and that the borders are made up of puncta closely resembling grains of cayenne pepper, although perhaps of a somewhat darker tint. He also refers to the telangiectatic appearance of some of the spots.

Discussion.—Dr. H. G. ADAMSON said he admitted the resemblance of this condition to Schamberg's disease, but the distribution was unusual and it had not the brick-red colour shown in that disease.

Dr. J. H. SEQUEIRA (President) said that Dr. Adamson and he each had a case of a family in which two members were affected with the condition; it was confined to the legs, and the cases had been watched for a long time.

Dr. G. B. DOWLING said a case of Schamberg's disease, that he showed at the last meeting but one of the Section,¹ had the condition on the arm above the elbow as well as a patch on the forearm.

A Case of Mixed Arsenical and Bromide Eruption.

By HALDIN DAVIS, M.B., F.R.C.S.

THE patient, a lady aged about 40, was sent to me by Dr. Edythe Lindsay, of Aldershot. All she complained of was a small warty lesion on the inner side of the right knee, with a somewhat cribriform surface from which a certain quantity of pus oozed. There was a history that bromide had been taken for some time, and I ascribed this lesion to the effect of that drug. Bromide is well known occasionally to cause a single lesion only, but as that is somewhat unusual I inquired whether she had any other "spots" elsewhere on the skin. She informed me that there were some on the lower part of the abdomen, and on examination I found there the typical rain-drop pigmentation, in the midst of which were two erythematous plaques of keratosis. There was also another patch of keratosis on the right shin. The appearance of these lesions was so characteristic of arsenical poisoning that I was sure she must have been taking arsenic. I then found that so long ago as 1902 she had consulted the late Sir William Gowers for epilepsy, and that ever since then she had been using his prescription and taking three minims of liquor arsenicalis three times a day. In addition to the lesions mentioned above she has also typical keratosis of the palms and soles, with tiny warts round the sweat follicles. She has entirely lost her sense of smell for the last eight years, and frequently suffers from tingling sensations, which are, no doubt, due to some slight degree of peripheral neuritis. She saw me originally a month ago, and since then she has discontinued the arsenic, but has continued to take bromide. It is interesting to note that the warts on the hands and feet have already begun to diminish in size, and that the surface of the palms and soles is less like that of a nutmeg grater. On the other hand, the bromide lesion is rather worse. Dr. Parkes Weber has just suggested to me that probably the taking of the arsenic had prevented the bromide from having its full effect.

Discussion.—Dr. H. C. SEMON said he had had two cases of arsenical dermatitis due to taking arsenic by the mouth, in one case for fourteen years without reference to a doctor, and in the other case for five years. He had published a report of the first case in the *British Medical Journal*² three years ago; in this case an epithelioma developed on the foot, necessitating amputation. In this patient the arsenical keratosis still persisted, in spite of the fact that the man had not taken arsenic for several years, and he (the speaker) was

¹ *Proceedings*, 1925-26, xix (Sect. Derm.), p. 1.

² "Arsenical Keratosis followed by Cancer," *Brit. Med. Journ.*, 1922, ii, p. 975.

periodically destroying fresh keratomata. He called Mr. Haldin Davis's attention to a paper in the *American Archives of Dermatology*, mentioning that common salt, 60 gr. a day, rapidly improved the effect produced by the bromide.

Dr. G. PERNET remarked that in conversation Mr. Haldin Davis mentioned the possibility of the development of epithelioma. He (the speaker) had recorded in 1901 a case of epithelioma of the hand which supervened in a patient who had taken arsenic for many years for psoriasis.¹ Part of the hand had to be amputated.

Dr. W. J. O'DONOVAN said he was struck by the similarity of the raised and roughened patch on the right lower abdomen to those seen in increasingly numerous cases of "Bowen's" pre-cancerous dermatitis.

Dr. J. H. SEQUEIRA (President) said that a very interesting case of carcinoma developing on chronic arsenic poisoning was recorded some years ago by Dr. G. R. Hamilton, who was at one time his (Dr. Sequeira's) clinical assistant.² That patient had taken arsenic for psoriasis for thirty-six years, and there was a typical keratosis of the palms and soles, and a carcinoma had developed on the right arm. It was remarkable how long such a result took to develop. The same experience was found in cases of arsenic cancer developing in workers in arsenic, such as in sheep-dip, cases of which were described by Dr. O'Donovan some time back.³

Mr. HALDIN DAVIS (in reply) said that one of the patches on this patient's abdomen and another on the shin showed appearances which, he thought, were comparable to the patches found in Bowen's pre-cancerous dermatoses.

Sections illustrating Histology of Xanthomatous Infiltration of Tendons.

Shown by G. B. DOWLING, M.D.

THE case from which these sections are taken was previously shown by me at the Meeting of the Section on February 21, 1924.⁴ The patient was a Polish Jewess, aged 28, suffering from xanthomatous infiltration of the tendo Achillis of both legs, and xanthoma tuberosum of both elbows. She was originally under the care of Mr. Robert Ollerenshaw at the Salford Royal Infirmary in 1920, who operated upon the tendons, reducing their thickness by paring them down. An account of this case was published by him in 1923 (*British Journal of Surgery*, 1923, p. 466).

While under my care during the last two years, the blood cholesterol has fallen from 0.6 to 0.3 per cent., presumably as a result of dieting. In spite of this, however, the infiltration of the tendons has gradually progressed, and the tendons on the dorsum of the hands have also become infiltrated. As the left tendo Achillis had become very thick and was interfering with walking, Mr. Tyrrell Gray removed it recently and transplanted a portion of the ilio-tibial band.

The specimens shown are:—

(1) A frozen section stained with hæmatoxylin and Sudan III, showing dense infiltration of the tendon with cholesterol and fat-laden cells. The fibres are split apart and in places are broken up by the infiltration.

(2) A section stained with hæmatoxylin and eosin.

(3) A section of xanthoma tuberosum of the skin from another case for comparison.

These sections were kindly prepared for me by Dr. R. R. Elworthy, with whom I have studied them. There are two points of importance relating to the histological appearances:—

¹ Radcliffe-Crocker and Pernet, "Epithelioma Supervening on Arsenical Keratosis," *Brit. Med. Journ.*, 1901, ii, p. 864. See also R. J. Pye-Smith, "Arsenic Cancer," *Proceedings*, 1913, vi (Clin. Sect.), p. 229.

² G. R. Hamilton, "Arsenical Keratosis and Epithelioma," *Brit. Journ. Derm.*, xxxiii, p. 15.

³ W. J. O'Donovan, "Arsenic Cancer of Occupational Origin," *ibid.*, xxxv, p. 477.

⁴ *Proceedings*, 1924, xvii (Sect. Derm.), p. 64.

(1) Complete absence of giant cells in the tendon tumour, which proves that this condition is distinct from xanthomyelosarcoma.

(2) The origin of the foamy cell.

In any portion of these sections, showing a moderately dense collection of foamy cells, we cannot help being struck by the fact that there are two kinds of cell, one the precursor of the other. (1) The foamy cell, often with pyknotic nucleus and cytoplasm distended with cholesterol and fat, looking very like a fully-charged sebaceous gland cell; (2) its precursor, a young cell with a large darkly-stained nucleus, generally ovoid in shape and arranged in small, quite dense collections, often about the centre of a mass of foamy cells. They resemble somewhat closely the young cells at the periphery of a sebaceous gland. All stages between this and the fully-developed foamy cell can be seen. The question of interest is the origin of these cells. Dr. Parkes Weber has stated that they belong to Metchnikoff's macrophages, as distinct from fibroblasts, and that they have adventitiously taken on the function of the phagocytosis of cholesterol. As xanthoma deposits are found only in connective tissue—e.g., the corium, connective tissue of tendons, scar tissue, glial tissue, particularly in avascular tissue—it seems to me more probable that these cells, which are picking up cholesterol, are identical with those which go to form young connective tissue. The question arises whether any distinction can be proved to exist between Metchnikoff's macrophages or phagocytic interstitial cells and those which develop into new connective tissue. I should like to suggest that they are identical cells which have originally no specialized function, but will do anything that may be required of them.

Dr. F. PARKES WEBER said he thought that there was a question whether cells of the Metchnikoff macrophage class (the histiocytes of Aschoff) might not be allied to cells of the fibroblast class. Recently Harvey Cushing had declared himself to be in favour of that view, for he suggested that the dura mater tumours, termed "dural endotheliomata" or "meningiomas," were derived from the meningocytes, which were phagocytic cells like the histiocytes or macrophages. Cushing thought that in these meningiomas fibroid tissue was developed from cells of the histiocyte class.

Case of Parapsoriasis (Brocq).

By G. B. DOWLING, M.D.

WOMAN, aged 28. Duration: four years. She states that the condition almost clears up in summer and recurs each winter. The case is of mixed type showing lesions of parapsoriasis guttata, some of the type parapsoriasis lichenoides giving the impression of slight atrophy, while some are irregular patches of brownish colour of the type parapsoriasis in patches. The disease is present upon the arms, legs and feet only. A point of some interest is that the lesions are present upon the dorsum of feet, for Brocq originally stated that the hands, feet and face were unaffected. I recently had a case of parapsoriasis guttata type in which feet, face and hands were all affected.

Case of Schamberg's Disease.

By G. B. DOWLING, M.D.

BOY, aged 8. Duration: 9 months. Distribution: one elbow and forearm and both legs. The only reason for showing this case is to demonstrate a transverse linear patch of the disease practically encircling the right leg, evidently caused by pressure of the garter.

Case of Lupus and Congenital Syphilis.

By W. J. O'DONOVAN, M.D.

R. A., AGED 16. Father killed at Gallipoli, 1915. Mother alive and well. Patient has an oval patch of lupus vulgaris with scarring immediately below symphysis menti, which, he says, followed a fall on the chin in 1918, and was treated locally by two applications of radium at Portsmouth.

There are numerous shallow radiating scars around mouth and nose. He complains of poor vision and has worn glasses for four years.

Mr. Charles Goulden reports that there is bilateral interstitial keratitis and disseminated choroiditis, with consecutive optic atrophy, and a large patch of choroiditis near the left macula.

The Wassermann reaction is negative, but this may be accounted for by two years of "injections" at Portsmouth, 1918-20.

The report from the Dental Department, London Hospital, is as follows:—

Incisors.—The upper left central incisor shows the following typical appearances. It is conical in shape and narrows towards the cutting edge, which is notched and shows a fair amount of attrition. One might have expected that the eruption of the upper right central incisor had been delayed (delayed eruption being not an unusual feature in these cases) because the patient does not remember having had the tooth removed, but a radiograph shows its absence, pointing to almost certain extraction at an earlier date. The upper lateral incisors are normal in shape and size.

The four lower incisors are small and conical and typical in appearance, the lower left lateral showing most attrition upon its cutting edge. Calcification is apparently good.

Canines.—The canines in this case are also affected, and those on the right side present a well-marked circumferential notch near the tip of the crown. The left canines show only the outline of the notch in each case, the central tip of enamel having disappeared through attrition.

Molars.—The first permanent molars with the exception of the right upper have been extracted at a previous date, but this remaining tooth is rather smaller than the normal, and has a typical dome-shaped crown, the biting surface of which is of an irregular pattern. This tooth is at present being treated. All the other teeth are normal in character. The bite is slightly opened in the incisor region, and it is possible that there may be some imperfect development of the alveolar portion of the bone in this region; but again the open bite may be due to other local causes.

Case of Flat Rodent Ulcer.

By E. G. GRAHAM LITTLE, M.D.

I THINK this is an example of flat rodent ulcer, of which we have seen many cases recently. It is on the cheek of a man aged 42. It has steadily progressed without retrogression for thirty years, and no other sites have been affected. When the patient first came, four weeks ago, there was an eczematous look on the surface; I did not see him then, I only saw him this morning for the first time. He has had three one-quarter pastille doses of X-rays, and it has rather altered the surface aspect. The extraordinary chronicity, the superficial character of the lesion and the colour of it seem to suggest the diagnosis I have mentioned.

Discussion.—Dr. G. H. LANCASHIRE said that so far as it was possible to see, the appearance of the patch struck him as having some resemblance to lupus vulgaris. He asked whether that was quite out of the question. There were nodules, and there was a long history of atrophy.

28 Roxburgh: *Multiple Idiopathic Pigment Sarcoma of Kaposi*

Dr. J. H. SEQUEIRA (President) said that he, too, thought that the question of lupus vulgaris should be considered. Perhaps Dr. Little would give the Section, later, an account of the biopsy (Dr. LITTLE: Yes).

Case of Multiple Idiopathic Pigment Sarcoma of Kaposi.

By A. C. ROXBURGH, M.D.

H. L., AGED 69. An English Jew. Has had psoriasis off and on since childhood. (Two of his nine children, now living, have psoriasis.) Thin old man, of slow movement and cerebration. Sent by his doctor to Mr. Gask at St. Bartholomew's Hospital early this month, and referred by Mr. Gask to Dr. Adamson. About four years ago patient began to notice purple blotches on hands and wrists; left ear became purple about July, 1924. Said to have had a "cyst" removed from in front of this ear a month previously. Nose became bluish same time as ear.

Left pinna now thickened, nodular, and purple; at the back of it are some soft cysts, up to $\frac{1}{4}$ in. diameter, containing clear fluid. A purple nodular growth extends forward $\frac{1}{2}$ in. on to cheek. Greater part of nose, especially tip, is swollen and purplish, though paler than ear. There are paler blotches on the sides of the tip. Small perforation in septum.

On backs of fingers and thumbs of both hands are purplish blotches, joined together across bases of fingers. Edges well defined and slightly raised, surface very slightly scaly. On backs of both hands and wrists are some similar blotches, $\frac{3}{4}$ in. to 2 in. in diameter. Similar lesions on outer sides of dorsa of both feet, on metatarso-phalangeal joint of right big toe and 2 in. above right ankle on inner side of leg. Patient states that patches are small to begin with and slowly increase in size.

He has also scattered lesions of psoriasis on trunk and limbs, especially on elbows and backs of forearms.

Blood count, December 16: Red cells 4,430,000, white cells 13,000. Differential: Polymorphs 6,630, lymphocytes 5,980, large mononuclears 260, eosinophils 130.

Radiograms of the small bones of the hands and feet show none of the clear areas which one would expect if the case were one of lupus pernio, and I do not think that the condition of the ear could be explained by this diagnosis either.

Section (shown) from the lesion on the back of right wrist shows thickening of the prickle-cell, granular and horny layers, but the most striking change is a great hyperplasia of capillaries in the reticular layer of the dermis, especially around the sweat glands and hair follicles, along with some associated cellular infiltration. A large number of the infiltrating cells are plasma cells, and there are some mast cells. No giant cells or tubercle-formation visible. There is some degeneration of the collagen. No visible hæmorrhages. Some pigment is visible in the deepest part of the section, partly intra-, partly extra-cellular. The appearances of the section seem to correspond much more closely with those described in the cases of Kaposi's "sarcoma," published by Sequeira and by MacLeod, than with those of lupus pernio.

Dr. J. H. SEQUEIRA (President) said that the earliest description, in this country, of Kaposi's disease emanated from Sir Jonathan Hutchinson, who described it as "symmetrical purple congestion of the extremities," and that description applied well to the present case. The only feature which was unusual was the condition of the ear, and he would like to see sections of the lesion there.

(Dr. ROXBURGH agreed to obtain the sections asked for by the President.)

Case for Diagnosis.

By W. N. GOLDSCHMIDT, B.Ch.

PATIENT, a boy, aged 19, upon the inner side of whose thigh spots began to erupt in August last. They did not then give rise to any symptoms, and he has never suffered from subjective symptoms. The spots were at first red, later they turned a lilac colour, and finally became brownish; yet the oldest lesions still have a lilac tint. They have spread to the trunk, abdomen and arms; they do not increase in size much beyond that of a pea, and do not coalesce. Apparently they have never risen above the skin, and it is impossible to evoke an urticarial reaction. Some new lesions still continue to appear. The question is whether the condition is urticaria pigmentosa, but there is no evidence of urticaria clinically. The distribution is unusual. The grouping reminds one of tertiary syphilis, but the Wassermann reaction is negative, and there is no scarring. Histologically there is very marked œdema of the papillary layer, to which this œdema is almost confined. But a few prickle-cells are also œdematous. There are no mast-cells and no hæmosiderin can be demonstrated. Sections stained with neutral red show some aggregations of cells containing melanin granules.

The patient's eyes look watery and puffy, but the urine is quite normal. He has, however, several very carious teeth.

Discussion.—Dr. A. M. H. GRAY said he was at a loss to make a diagnosis in this case, but the colour reminded him of a case which Dr. Graham Little had shown some years ago. He asked Dr. Little at the time whether he thought it was a type of case described by Americans as urticaria pigmentosa, but which showed no increase in the mast-cells. Since then, the late Dr. Hannay had written on urticaria pigmentosa, and said he thought certain of these cases did not show an increase in the mast-cells but that it was impossible to differentiate clinically those which showed an increase from those which did not. The distribution was not the usual one prevailing in this condition.

Dr. GRAHAM LITTLE said he did not think this case suggested urticaria pigmentosa; there was no turgescence after prolonged friction, and he thought the colour differed from that of the disease just mentioned. This was an adult case, and the adult cases of the condition he had seen had shown a remarkable distribution over the extremities, especially the forearm. This seemed more like a pigmentation left by a preceding lesion of some kind. With regard to the presence of mast-cells, he was doubtful about cases in which mast-cells were not present. He had had a typical case of urticaria pigmentosa in which there were no mast-cells; the eruption was on the forearm.

Case of Congenital Ichthyosiform Erythroderma (Brocq).

By J. E. M. WIGLEY, M.B.

THE patient is an extremely healthy looking little girl, 2 years of age.

Family History.—Negative.

The present condition was first noticed at the age of 5 months. There is a dry, thickened condition of the skin of the arms and legs (chiefly affecting the flexor surfaces, including the flexure of the elbows and knees), erythematous and hyperkeratotic plaques on the buttocks and thighs, and a dry scaly condition of the face and scalp. No other congenital defects. There has been no irritation during her three weeks' stay in hospital. No evidence of asthma or any other chest affection. Wassermann reaction negative.

Histological section shows hyperkeratosis, with some dilatation of blood-vessels.

Dr. F. PARKES WEBER asked whether this was not the kind of case which had been described as congenital erythrodermatodermia amongst other terms. This might be localized to particular parts, and might be regarded as a nevus condition, and was in the present case more or less symmetrical in distribution. The ichthyotic skin was seen obviously, by ordinary naked-eye examination, to be on a telangiectatic basis.

[January 21, 1926.]

Two Cases of Cheilitis Exfoliativa.

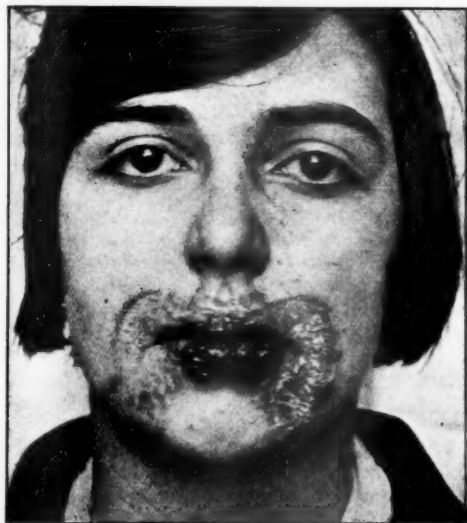
By ROBERT GIBSON, M.D. (Manchester).

Case I.—A. P., aged 44, married, developed a crack in the centre of the lower lip at Christmas, 1924, and by May, 1925, the trouble involved the whole of the lower and the centre of the upper lip. When she was seen in July there was a thick blackish crust covering the lower lip, which, on removal of the crust, appeared red and granular, but not ulcerated. Both lips were painful and protuberant, thus interfering with opening of the mouth and the taking of solid food. General health good. Teeth artificial and in good condition. Mild seborrhœa capitis. Wassermann reaction negative.

Treatment, including exposure to X-rays, has proved unsatisfactory.

Case II.—D. O., aged 20, unmarried. The disease began with a crack in the centre of the upper lip four years ago. She was constantly picking at it. The lesion gradually spread, and a year later the lower lip became involved, and when patient was seen in January, 1925, the state of the lower lip was worse than that of the upper, as it was covered with a dark, hard scab sodden at the inner edge. She complains of a burning in the lips, but no pain. General health good; teeth perfect. Wassermann negative, a mild seborrhœa capitis is present.

Treatment, as in the first case, has proved unsatisfactory.



Postscript.—The illustration is that of another case which was reported at the Meeting. The photograph was taken after the administration of X-rays. This case cleared. I am indebted to Dr. Savatard for permission to report it.

Discussion.—Dr. J. H. SEQUEIRA (President) said he agreed that these cases were very difficult to cure. X-ray treatment was successful in some cases. But the etiology of the condition was not known, therefore treatment in these cases could only be in the nature of an experiment.

Mr. T. P. BEDDOES said that in many cases of this condition there was an associated gastric disturbance, and it was extremely useful not only to give mouth-washes, but also to attend to the state of the naso-pharynx and to that of the digestive tract generally. A further point to be noted was that the continual movement of the lips perpetuated the condition. The making of tiny transverse incisions kept the lips at rest and aided healing, acting like scarification. At the first visit, the lips were painted with cocaine and lightly cut with a lancet. At the next visit the lancet was used without cocaine, and the patient was usually expert enough to perform the operation, and continued to do so at home every third or second day. So far as he knew, those were the two most successful treatments.

Case of Vagabond's Disease.

By A. WHITFIELD, M.D.

THE patient, a girl, was sent to us at the hospital from the infirmary four weeks ago. She showed pigmentation rather more marked than at present. Apparently she is mentally deficient, therefore the history I have written down is probably inaccurate. She appeared at the infirmary in what they called there an indescribable condition of lousiness. She still had scabies when she came to the hospital. She is naturally dark-skinned, but she shows this extraordinary pigmentation, and on the shoulders it is mostly surrounding scratch-marks and tears of the skin. She was a mass of tears all over the body, and there was a universal hyperidrosis with vesicles, some of them due to the scabies. I obtained the history that two years ago she quarrelled with her parents and left her home. Most of the time since she has been practically starving, and has been sleeping in the streets. She has, in fact, been under conditions which develop what is known in Paris as "vagabond's disease." The question arises whether this is all the toxic effect of the intense parasitism, or whether it is, in part at least, arsenical. She gives no history of having had injections of arsenic compounds, but her Wassermann reaction is strongly positive. We have had her urine carefully examined for arsenic and it yielded none. My tentative diagnosis is that it is all vagabond's disease, though I am prepared to admit she may have had arsenic.

Two Cases of Tuberculosis of the Buttocks.

By S. E. DORE, M.D.

ONE patient, a man aged 48, is a case of typical lupus verrucosus of the buttocks, and the other, a man aged 43, has a lesion which is more of the tuberculous gumma type. In both cases the eruption began in the year 1915, following an operation for fistula-in-ano. Mr. Adams, of St. Thomas's Hospital, tells me that only 15 per cent. of the cases of fistula-in-ano are tuberculous, but I think there is no doubt that both my cases are tuberculous, although it may be interesting to mention that the first case, in which there is a large infiltrated mass in the right buttock, was diagnosed as a typical gummatous syphilide, but all the tests have been negative. Another interesting feature of the two cases is that the first man was a camel rider in Egypt, and it seems probable that tubercle bacilli from the fistula infected the surrounding skin. In the case of the other man there is a history of his riding a pony bare-backed some years before his fistula appeared.

Dr. J. H. SEQUEIRA (President) said these cases were of considerable interest. He had seen several cases of typical lupus of the buttock, but the lupus usually began in childhood. He had considered that abrasions of the skin caused by friction had allowed the organisms to enter and set up the condition. In association with anal fistula he had usually seen a more acute form of tuberculosis, and this occurred in moribund patients suffering from active tuberculosis of the alimentary tract. Dr. Dore's two cases were of particular interest because of the age at which the lupus began to appear.

Sections from (?) Case of Multiple Idiopathic Pigment Sarcoma of Kaposi exhibited at the last Meeting, December 17, 1925.¹

By A. C. ROXBURGH, M.D.

I WAS asked by the President at the last meeting to take sections from the ear of the case of Kaposi's sarcoma I then showed. I took sections from the nodule in front of left ear, and they are now under the microscope. I think they support the diagnosis of Kaposi's sarcoma. In the corium there is a mass consisting of strands of fibrous tissue running in different directions and containing a considerable number of nuclei; between the strands are an immense number of dilated blood-spaces, the majority lined with endothelium, the whole constituting a sort of sponge. In places there is a massive cellular infiltration, about 50 per cent. plasma cells, especially about some of the hair follicles and in the deeper parts of the section. There are several hæmorrhages, one larger and several smaller, in the area of the section and a fair amount of pigment, chiefly extracellular.

(?) Case of Mycosis Fungoides (Tumeurs d'Emblée Type).

By H. C. SEMON, M.D.

MEMBERS will remember that I showed this case at the last meeting of the Section a month ago,² as one of Kaposi's idiopathic multiple pigmented sarcoma.

There has been almost complete involution of all the tumours within that time, after only one dose of X-rays, so that the diagnosis put forward by Dr. Pernet, Dr. MacCormac and the President, of mycosis fungoides (tumeurs d'émblée type), receives very strong support. I beg leave, therefore, to withdraw my original opinion.

Discussion.—Dr. J. H. SEQUEIRA (President) said that Dr. Semon's remarks were particularly interesting because of the therapeutic test. It was agreed that there was nothing more remarkable than the way in which the tumours of mycosis fungoides melted away under moderate doses of X-rays.

Dr. S. E. DORE asked whether the fact of the tumours clearing up under X-rays could be accepted as proof that the condition was mycosis fungoides. Did not some of the sarcomata clear up with equal rapidity under that treatment? He would not have thought the fact stated was a sufficient proof of the diagnosis.

Dr. F. PARKES WEBER said he considered that the balance of evidence was in favour of this case being a form of round-celled sarcoma. Some cases of sarcomata yielded wonderfully well to X-rays, as, for instance, certain mediastinal tumours. He still believed the sections to be quite typical of round-celled sarcoma. The glands in the skin might be only infiltrated and not destroyed, yet that was not incompatible with the microscopical diagnosis of sarcoma.

Dr. SEMON (in reply) said that he thought the balance of evidence very much in favour of mycosis fungoides, although two out of the four pathologists consulted regarded the section as a round-celled sarcoma rather than one belonging to the group of infective granulomata. For his own part he (Dr. Semon) could not imagine a round-celled sarcoma starting symmetrically on the extremities, as in this case, the signs of which seemed to point definitely to some general toxic or infective process.

¹ See *Proceedings*, 1925-26, xix (Sect. Derm.) p. 28.

² See *Proceedings*, 1925-26, xix (Sect. Derm.), p. 21.

Section of Dermatology.

President—Dr. J. H. SEQUEIRA.

Urticaria Pigmentosa in an Adult.

By ERNEST MALLAM, M.D.

PATIENT, female, aged 43, married. The eruption first appeared when she was aged 41; it is situated on the arms—especially the forearms and backs of the hands—the inner side of the legs, the dorsum of the feet, and, to a slight extent, the trunk.

As regards its main features the case illustrates all the six characteristics enumerated by Dr. Hannay in his paper in the *British Journal of Dermatology and Syphilis* in January, 1925, as supposedly commoner in adult cases: (1) The urticaria is mild; (2) the lesions are small; (3) the eruption is macular; (4) it is not of the xanthalasmoid type; (5) the onset is after puberty; (6) mast-cells are absent, though he proves that not any of these points is essential.

Cases of Dermatitis Scrofulosa.

By H. W. BARBER, M.B., and G. B. DOWLING, M.D.

WE are showing these cases because since one of us (H. W. B.), in conjunction with Dr. Attwater and Dr. Marshall, brought some similar ones before this Section in December, 1920 (Barber, Attwater and Marshall, *British Journal of Dermatology*, xxxiii, April, 1921, p. 154), there has been a new development, which, we think, confirms the view then put forward that the eruption is of tuberculous origin, and doubtless corresponds with Boeck's "eczema scrofulosorum." This view was at that time contested, chiefly by Dr. Whitfield, who claimed the eruption to be the same as his "discoïd eczema," and by Dr. Adamson (Adamson, *British Journal of Dermatology*, xx, April, 1908, p. 109), who recognized it as corresponding to that described by him as "a form of chronic superficial dermatitis in circumscribed patches with symmetrical distribution, occurring in children," which he did not consider to have any connexion with tuberculosis.

We would here state that the eruption we call "dermatitis scrofulosa" is different from Dr. Whitfield's discoïd eczema, which, we think he will admit, is the same as Sabouraud's impetigo pityroides. Thus, to quote Dr. Whitfield's own words (*British Journal of Dermatology*, 1900, p. 406):—

"The disease occurs in the form of small, well-defined discs, varying in size from that of a lentil to that of a shilling, on the faces of young children. It is situated chiefly upon the cheeks, chin and neck, and has a rather pronounced predilection for the skin round the mouth, here often occurring in a sheet of considerable size and losing its circular outline. The more detailed examination of a single patch shows that it is primarily a very superficial disturbance of the epidermis. The horny layer is broken up by a series of fissures, giving rise to an appearance not unlike that of crêpe. The scales thus formed are usually more or less fusiform in shape, the direction of the fissures being the result of the movements and tension of the skin. Attempted removal of the scales shows that they are rather strongly adherent, since it is almost impossible to lift one off without breaking it up, and slight hæmorrhage usually results from the use of force. The patches are almost absolutely flat and give no sensation of resistance to the finger, the only thing noticed being the slight harshness. Unless interfered with in some way there is scarcely

any hyperæmic redness, but on scraping them or washing them they at once flush up and become bright scarlet. In the majority of cases the scalp is unaffected, but I have noted the presence of pityriasis in some. Occasionally the eruption appears to generalize, and then shows a marked predilection for the extensor surfaces of the arms and legs, and also becomes a typically follicular disease."

Now dermatitis scrofulosa occurs on the limbs and trunk rather than on the face; when it does occur on the face the patches have no predilection for the skin round the mouth, they tend to be larger than those of "discoïd eczema," they are not fissured, unless irritated by soap and water, and they have a characteristic tint which varies from a pinkish-fawn colour to a dirty brownish hue. The scales are larger and more flaky and fairly easily detached; the patches are not, as a rule, circular, but are oval or irregular, and may form large sheets, particularly below the margin of the hair on the temples, and on the limbs.

With regard to Dr. Adamson's cases the resemblance to our own is much greater, and we are inclined to think that some, at any rate, of those he has so well described are identical.

Some time ago one of us (H. W. B.) was asked to see a boy in the medical wards at Guy's Hospital, and was shown scaly patches on one forearm which were quite typical of dermatitis scrofulosa. They had developed on the scratches to which tuberculin had been applied for von Pirquet's reaction; the boy was suffering from tuberculous peritonitis. Since then one of us (G. B. D.) has done von Pirquet's tests on a series of cases of dermatitis scrofulosa, and fresh patches of the eruption have been produced in this way.

Apart from these observations, since the original cases were shown in 1920 (by H. W. B.) we have seen mixed cases of this eruption and typical lichen scrofulosorum. One private case impressed us very much; a boy, whom one of us (H. W. B.) had treated in infancy for eczema, was brought again with an acute outbreak, on the trunk and limbs, of dermatitis scrofulosa of ten days' duration, and within a week he had developed a characteristic eruption of lichen scrofulosorum. He saw Dr. J. J. Perkins, who agreed that the boy, although apparently well, had active generalized tuberculous adenitis.

It must be remembered that Dr. Marshall, who was entirely sceptical at first, found demonstrable evidence of tuberculous infection in 82 per cent. of the original fifty cases (H. W. B.) collected by Dr. Attwater.

Our own view is that dermatitis scrofulosa corresponds to the eczematoid trichophyotide described by Jadassohn and Guth, and that it is an eczematoid reaction produced by sensitization of the epidermis to tuberculin. The reproduction of the eruption by the application of tuberculin is in favour of this view. An interesting point is the rapidity with which the lesions disappear under the influence of ultra-violet light.

Discussion.—Dr. A. WHITFIELD said he was by no means convinced that the lesions were tuberculous. He was, however, quite convinced that Boeck's eczema scrofulosorum was identical with what he (the speaker) had provisionally named discoïd eczema, for the simple reason that Boeck and himself had discussed the matter in the presence of cases and Boeck had identified as eczema scrofulosorum what he (Dr. Whitfield) claimed as discoïd eczema.

He (the speaker) did not think that the scaling after tuberculin inoculation was a specific reaction. Inoculation of tuberculin into the skin of a tuberculous child produced a toxic erythema because the tuberculin acted as an irritant. When this erythema faded it was followed by scaling consequent on the disturbed nutrition of the skin. It was analogous to the scaling which one commonly saw in patients who were so sensitive to a mosquito's poison that a puncture would be followed by a widespread erythema. This was often followed by a chappy scaling and sometimes led to an actual eczematization.

As regards his description Dr. Barber had quoted his (the speaker's) description of the eruption as it occurred on the face, but he (Dr. Whitfield) had expressly stated that when it

occurred in the extremities it differed in character and was beset with little pin-point papulovesicles which he (the speaker) had believed to be follicular in site until Dr. Adamson had shown him that they were not actually at the site of follicles. Most of the children shown by Dr. Barber had been washed habitually with one of the incriminated soaps. Dr. Dowling had said that these cases which they believed to be tuberculous had given a positive von Pirquet reaction. Could he tell them how many cases deemed to be non-tuberculous had been tested and what was the result?

Dr. H. G. ADAMSON said he recognized these cases as of the same character as those which he (the speaker) had described in 1908 as "a form of chronic superficial dermatitis in circumscribed patches with symmetrical distribution, occurring in children." He (the speaker) had then discussed the diagnosis from "patchy eczema," eczema seborrhoicum, lichen scrofulosorum, eczema scrofulosorum (Boeck), parapsoriasis (Brocq), and parakeratosis psoriasiformis (Brocq). He was interested in Dr. Barber's view that they were of tuberculous origin, though he (Dr. Adamson) still felt that they were of an independent origin. Histologically they were certainly different from lichen scrofulosorum and he had watched several cases for many years and none had shown tuberculous lesions of any sort. He was gratified to hear Dr. Dowling say that he regarded this affection as an entity.

Dr. DOWLING (in reply) said that he marked certain cases as characteristic, and they all turned out to be positive. He had investigated eight cases. Three others he regarded as doubtful, or as not the same thing, and the reaction in all three happened to be negative. A larger series was of course wanted.

Dr. J. H. SEQUEIRA (President) said that as some of the cases of presumed dermatitis scrofulosa were rapidly cured by light, it would be a useful control to submit the cases described by Dr. Adamson and Dr. Whitfield to light treatment.

Dr. BARBER (in reply) said he could not find Professor Boeck's original article; what he knew about Boeck's eczema scrofulosorum he derived from hearsay and from text-books. The point made by Dr. Whitfield was a very good one: that one might expect to get much the same reaction after doing a von Pirquet or after a mosquito bite. But in the first case he saw the patch following the von Pirquet test was a large one and was typical of this eruption: there was also more inflammation a fortnight after than one would expect from merely scratching the skin. (Dr. WHITFIELD said he was not contending that these were not tuberculin reactions, but that tuberculin was not a poison except to a tuberculous patient, and to a normal person would cause no discomfort.) Dr. Whitfield had described the eruption as occurring on the trunk, whereas Dr. Adamson had said the eruption was rare on the trunk. He (the speaker) regarded it as an eczematoid reaction produced by sensitization of the epidermal cells to tuberculin, whereas lichen scrofulosorum was an acute follicular reaction. He recalled that Dr. Adamson had tested two of his cases for Calmette's reaction and in both cases the result had been negative.

Case of Confluent Lichen Nitidus.

By H. W. BARBER, M.B.

I AM showing this case because it differs considerably from my other cases of confluent lichen nitidus. When I first saw the patient I was for a few minutes in doubt as to whether the eruption was lichen nitidus or lichen planus, but decided on the former diagnosis, which has been confirmed by microscopical sections.

The patient, Mrs. R. W., aged 59, has had good health on the whole since childhood, except that she has for a long time suffered from asthma and bronchitis. The eruption began in June of last year, and was first noticed on the sole of the foot, the affected part being apparently scaly and fissured. This condition, however, had cleared up before she first came to my out-patient department, but I must remark here that on the palms and soles confluent lichen nitidus occurs, usually in the form of scaly, hyperkeratotic, dry and fissured patches, which are apt to be mistaken for chronic patches of eczematous dermatitis. The rash then appeared on the legs and later on the arms. I have not seen her for a fortnight until to-day. At that time the distribution and characters of the eruption were as follows:—

Arms.—Antecubital fossæ, only a few faint discrete papules. Isolated papules on the wrists rather resembling those of lichen planus. Along the ulnar borders of the forearms, several confluent patches.

Legs and Thighs.—Here the eruption is more profuse, particularly on the anterior aspects of the legs. There are confluent lilac-coloured patches on the knees, and below these the eruption is composed of isolated papules closely aggregated and small confluent patches, some of which are slightly scaly. There is a confluent lilac-coloured patch on the dorsum of one foot.

Abdomen and Groins.—A few more typical discrete papules are present.



There are no lesions on the buccal mucous membrane. The eruption in this case differs from that seen in my previous cases of the confluent type in the colour of the lesions, which recalls that of lichen planus, being of a lilac or violet tinge. Moreover, the pityriasiform appearance of the confluent patches, so characteristic in my other cases, is absent.

Histological Appearances.—I have shown serial sections from two biopsies, one made of a piece of skin including practically only one discrete papule, the other of a confluent patch. In the former the papule is seen as a more or less sharply circumscribed tuberculoid mass consisting of epithelioid cells and of round cells of the mononuclear type, which lie in between the epithelioid cells. In sections of the confluent patch there is a diffuse infiltration of the corium with the same types of

cells, with here and there a giant cell, and it is difficult to distinguish the original little circumscribed granulomata composing it.

A very striking feature is the way in which the infiltrate eats into the overlying epidermis, the rete cells becoming disintegrated and coming to lie actually in the infiltrate among the epithelioid and mononuclear cells. Kyrle and McDonagh emphasized this feature very clearly in their paper on lichen nitidus.

In the sections of a single papule the layers of rete cells above the granuloma will be seen to be thinned, but there may be hyper- and parakeratosis of the horny layer; in the interpapillary downgrowths, however, there may be acanthosis. This acanthosis is strongly marked in some sections from the confluent patch. There is no doubt that the granuloma begins around a blood-vessel, and in serial section it is possible to trace the evolution of a papule from a small perivascular cell-infiltration to a fully-formed granuloma lying just beneath the epidermis.

Case of Basal-celled Carcinoma of the Back, following a Mole. (Pagetoid Epithelioma of Darier.)

By H. W. BARBER, M.B.

I HAD hoped to show to-day a case of Bowen's pre-cancerous dermatosis in an old woman who has a patch of about two years' duration on the front of one leg. I hope to show her at the next meeting. At first I was doubtful whether the lesion was Bowen's disease or a kind of granuloma pyogenicum, but eventually decided on the former, and microscopical sections confirm this. I have brought some of the sections here in order that they may be compared with those of the case of basal-celled carcinoma which I have shown to-day.

This latter case I thought was also probably one of Bowen's dermatosis of an atypical kind, but the sections showed that I was wrong. The actual lesion, however, is clinically not unlike the patch in the case of Bowen's pre-cancerous dermatosis.

This patient is a married woman, aged 48, who was sent to me by Dr. Barbour, of Dulwich, suffering from a chronic lesion on the back, which did not yield to treatment. Her story is that in the area now occupied by the lesion, she had had a "mole" apparently since birth. Five years ago this was "rubbed off by her corset," leaving a sore place which would not heal; it apparently became for a time secondarily infected and discharged pus. Various applications were tried without effect except that the lesion dried up. An interesting point which she has noticed is that at her menstrual periods it invariably became inflamed and oozed, only to dry up again after the period. In October last year, however, the lesion became permanently sore and moist.

At the present time the appearance of the lesion differs very considerably from that presented on her first visit to me. At that time the surface was moist and covered with small papillomatous projections, and the outer part was crusted, so that no definite rolled edge was visible. Now it is clinically, as well as microscopically, clearly a case of basal-celled carcinoma. It is a roughly oval patch situated on the back at a level with the right iliac crest. It is about $1\frac{3}{4}$ in. in length and 1 in. in breadth. At the periphery the characteristic rolled edge can be seen. The surface is now dry and covered partly by scales and partly by dried crusts; there is obvious atrophy in this central part.

It is particularly unfortunate that I was not able to show the case of Bowen's disease this afternoon, so that it might be compared with this case. The fact that I at first mistook the latter for one of Bowen's dermatosis will prove an argument for those who hold that no sharp line can be drawn between these various forms

of epitheliomatous and pre-epitheliomatous conditions of the skin. This was the view put forward by Professor Bosellini in the paper he read here. I still, however, maintain that Bowen's dermatosis is a distinct entity, and has nothing whatever to do with the superficial erythematoid basal-celled carcinoma so well differentiated by Dr. Graham Little, Dr. Gray, and others. The first case I saw was, I believe, the first diagnosed in this country, and I recognized it from the picture of Bowen's first case; there were three plaques almost identical with that picture. Unfortunately there was already involvement of the glands draining the areas occupied by the patches, and, in spite of extensive removal of these by Mr. E. C. Hughes, the patient eventually died of squamous-celled carcinoma. The lesions in that case were unlike anything else, and could be recognized at a glance. Other cases, however, may not be typical, at any rate by the time the patient is seen by a dermatologist—as, for example, the one from which the sections submitted to-day were taken—and I agree with Mlle. Eliascheff (*Annales de Derm. et de Syph.*, July, 1923, Serie vi^e, iv, No. 7, p. 433), who says that it may be impossible, clinically, to make a differential diagnosis between Bowen's disease and some forms of pagetoid epithelioma, but the histology is absolutely distinct. You will see in the sections of the case of basal-celled carcinoma a few dyskeratotic cells lying chiefly in the rete at the upper level of the basal-celled downgrowths, but they are not nearly so numerous or so characteristic as in Bowen's disease, in which large masses of irregularly arranged, dyskeratotic Malpighian cells are seen.

A Case of Vitiligo with Addison's Disease.

By NORMAN BURGESS, M.B.Cantab.

A. A., MALE, aged 33, admitted to Guy's Hospital on August 24, 1925, under Dr. Herbert French, to whom I am indebted for permission to publish this case. Patient had suffered from furunculosis while in the Army; severe attack of influenza at end of 1918.

Present illness dates from October, 1919, when he first noticed dyspnoea on exertion; this progressed, and four years later he began to suffer at irregular periods from nausea, giddiness, exhaustion, faintness and flatulence. These attacks have persisted ever since, with intervals of freedom from symptoms. He has lost 2 st. in weight in the past two years, and has suffered from paræsthesia of the fingers and toes, and general hyperæsthesia of the skin.

In 1915 he noticed a dark area of pigmentation on the left side of the neck, but it was not until 1923 that he found he was becoming generally pigmented. In April, 1924, a patch of vitiligo appeared on the left side of the neck below the original patch of pigmentation. These areas of vitiligo have greatly increased in number lately. In February, 1925, he noticed that small black spots about the size of a pin's head and composed of local dense deposits of dark pigment, were becoming superimposed on the already pigmented skin. None of these spots occurred on areas of vitiligo. At this time the patient was admitted to St. Bartholomew's Hospital with symptoms of hyperthyroidism. He had then a basal metabolic rate of 32 per cent. above the normal. On admission to Guy's Hospital in October, 1925, the skin was deeply pigmented, especially over the lower abdomen and becoming somewhat less so in the direction of the head and feet; the soles of the feet and the scalp were normal in colour. The pigmentation was most strongly marked in the areolæ of the nipples and the scrotum. The lower part of the back was mottled, the light areas corresponding to the summits of hair papillæ. There were also small, irregular deposits of black pigment not raised above the surface. Patches of pigmentation were present on the palate and in the left sclerotic. In addition there were extensive

patches of vitiligo most marked on the left side of the neck and trunk. Springing equally from the leukodermic and pigmented areas were fine downy hairs.

Blood-pressure: 93 mm. systolic; 45 mm. diastolic. Some exophthalmos, and fine tremors of fingers; skin somewhat hyperæsthetic. Adrenalin produced a greater rise of blood-pressure in the patient than in normal persons.

Blood-count: Hæmoglobin 69 per cent.; red cells 3,760,000; colour index 0.92; red cells normal in appearance and fragility.

White cells 6,050: Polymorphonuclears 48 per cent.; lymphocytes 38.5 per cent.; large hyalines 9.7 per cent.; eosinophils 2.5 per cent.; basophils 0.5 per cent.; myelocytes 0.75 per cent.

The Wassermann, complement-fixation against tubercle, and Van den Bergh's reactions were negative.

Patient was found to have complete achlorhydria. X-ray examination of the alimentary tract revealed no abnormality. Investigation of the feces, urine and ductless glands gave negative results. The basal metabolic rate was normal. No shadows were cast by the suprarenal bodies by X-ray. No active disease was found on X-ray examination of the chest. The muscular power of the hands was much below normal, but the muscles did not tire more easily than in normal controls; the electrical reactions were normal, but the dextrose tolerance test gave a result resembling that seen in cases of myasthenia gravis. The lævulose test showed slight hepatic deficiency.

The colour of the skin corresponded to a mixture of blue 3.0, red 5.0 and yellow 3.0 on the tintometer standard scale.

As the patient could not be made to sweat by the hot-air bath alone pilocarpine nitrate $\frac{1}{4}$ gr. was injected. The skin sweated uniformly, the patches of vitiligo sweating as much as the pigmented areas. A mustard plaster applied to an area of vitiligo had no effect on the white patch, but the surrounding area of pigmented skin on which the plaster had overlapped, peeled off later, leaving white skin beneath. This soon became replaced by a fresh layer of pigmented skin, showing that the pigment resided in the superficial layers only. While in hospital the patient suffered from attacks of nausea, giddiness, flatulence and diarrhœa, during which time the systolic blood-pressure was usually between 85 and 95 mm. He had intervals of freedom from symptoms; during these periods the systolic blood-pressure was above 100 mm. He was treated with adrenalin, at first by the mouth and later subcutaneously. The attacks continued and the intervals of freedom could not be ascribed to treatment.

In February, 1926, he began rapidly to lose ground, and, following an attack of tonsillitis, he died on March 19.

Unfortunately permission for an autopsy was refused.

The association of the attacks from which the patient suffered, with a low blood-pressure and pigmentation of the skin and palate, makes the diagnosis of Addison's disease almost certain. The case is recorded because of the rarity of the association of this disease with vitiligo. It seems probable that the hyperthyroidism, from which the patient was suffering in February, 1925, while in St. Bartholomew's Hospital, and traces of which could still be found in October of the same year when in Guy's, was secondary to, and possibly compensatory to, the Addison's disease.

Discussion.—Dr. F. PARKES WEBER said he would have preferred that this case should be labelled "Addison's disease, with hyperthyroidism (or Graves' disease) and vitiligo," because he considered Addison's disease the most important of the three conditions. Vitiligo was a very rare complication of Addison's disease by itself. In this case he suggested that the vitiligo was associated not so much with the Addison's disease as with the hyperthyroidism (or Graves' disease), with which it was not very rarely associated.

Dr. BARBER said that he agreed with Dr. Weber, because hyperthyroidism was associated with sympathetic irritation, whereas Addison's disease was associated with sympathetic

paralysis. In a case of extensive vitiligo associated with alopecia areata which he (the speaker) had investigated with Professor Pembrey, their experiments with a hot-air bath and pilocarpine were more striking than in this case; in their case they had seen a marked difference in the degree of sweating on the white patches as compared with the dark. But it was not always the same; in some experiments the white patches sweated more than the dark. Professor Pembrey explained that by saying that the patient had evidently some lesion of the sympathetic system of the irritative type.

Case of Syringocystadenoma.

By M. SYDNEY THOMSON, M.D.

THE patient, a single woman, aged 34, first attended the out-patient department of King's College Hospital on January 14, 1926. She then complained of an eruption on the scalp, which proved to be psoriasis and rapidly improved under routine treatment.

During examination certain additional lesions were noticed on the trunk. These were diagnosed by Dr. Whitfield as syringocystadenomata, an opinion confirmed by the histological picture. These "spots," of which there are now approximately two hundred, were first noticed by the patient about six years ago, when a large number appeared simultaneously. Four years later a fresh crop was added after an indefinite period of ill-health. Recently, still more lesions have become manifest, whilst all have apparently become somewhat larger and redder, these changes synchronizing with the onset of the psoriasis four months ago. Apart from these facts there is nothing of interest in the history either of the individual or of the family.

The lesions vary in size from that of a pin's head to that of a small pea. Each is slightly raised above the surrounding skin but has produced no clinical changes in the epidermis itself although they are all definitely attached to it. Whilst they are mostly seen as discrete nodules, some are collected into small groups. Occasionally a line is formed, looking like a short string of beads. Although they are widely distributed over the trunk and the immediately adjacent parts of the limbs and neck, they are most thickly aggregated over the lower abdomen. The largest and most luxuriant lesions, on the other hand, are found in the axillae. They are certainly not follicular in origin nor are they distributed along the lines of cleavage. They do not appear to be related to any particular areas of distribution of the cutaneous nerves.

The sections show an unaltered epithelium, whilst the corium, in the upper part of which the new growth is situated, itself seems to be unchanged except for a slight increase in the density of the fibrous tissue. Those sections which were stained with Pappenheim, and for the differentiation of elastic tissue, gave no additional information. This is contrary to the opinion of Richard Sutton, who holds that the elastic tissue is somewhat reduced in amount although encircling the cysts. Small masses of epithelium are scattered throughout the cutis and tubules. These strands are sometimes wavy and have a definite double row of cells. In other places there are definite cystic spaces which also have similar epithelial walls. Here and there are seen spaces round which the cells are more thickly disposed, those towards the centre then being apparently degenerate. This change may account for some of the material which can be seen within the lumina, and is in agreement with the observations of Theodor Brauns, published in the *Archiv* in 1903.¹ He, too, could find no dilatation of the mouths of the ducts nor any sign of comedone formation. In these particular sections no signs of true sweat-glands were found in the immediate neighbourhood of the growths, and this fact is probably in favour of the hypothesis that they are resulting from the transformation of epithelial rests. Certainly the history of this particular case is very similar to that given by some patients who complain of the sudden appearance of many pigmented naevi.

¹*Archiv. f. Derm. u. Syph* 1903, lxiv, p. 347.

Discussion.—Dr. G. PERNET said that in 1907 he had published¹ a note on the histology of this condition under the title of "Nævi cystepitheliomatosi disseminati." Syringocystadenomata is a better name for what used to be called lymphangioma tuberosum multiplex. He showed the lesions were connected with the sweat-glands. In 1918 he (Dr. Pernet) had shown² a case before the Section occurring in a female patient.

Dr. J. H. SEQUEIRA (President) said he agreed as to the unusual extent of the condition in this case. He had usually seen it limited to the triangle below the breasts and the upper part of the abdomen.

Dr. LOUIS SAVATARD said that he had seen, a few years ago, a case in which the lesions were as extensive in area as in this case, though with fewer tumours. The slides of his (Dr. Savatard's) case had shown an apparent increase in the fibrous tissue, and sweat-glands were present in the neighbourhood of the growth. He (the speaker) did not consider that their absence in the section shown was proof of the embryonic origin of these tumours.

Two Cases of Lupus Erythematosus.

By ERNEST G. FFRENCH, M.D., M.R.C.P.Lond.

THESE cases of lupus erythematosus are brought to show the contrast between the results of CO₂ treatment and X-ray treatment. I think that hitherto the X-ray treatment has been rather unsatisfactory in this condition; therefore we thought at St. Bartholomew's we would apply X-ray treatment to one side of the face, and CO₂ treatment to the other. The duration of both these cases was about eight years. The thin man came to us in October, 1924, and very soon afterwards I began X-ray treatment on one side, $\frac{1}{2}$ pastille every four weeks. He has had those doses ever since, to date, except that the last two doses were increased to $\frac{1}{2}$ pastille each. I began X-ray treatment on the other case last May, with the same dosages. I ask you to contrast the marked difference in the results of the two treatments.

Discussion.—Dr. DENNIS VINRACE said one of the patients had two ulcers on the right cheek, and asked what was their history. The patient said he had had CO₂ applied to that side, and that he thought the CO₂ had caused the damage. Was that at all likely? He (Dr. Vinrace) did not doubt the diagnosis, but it was an unusual case of lupus erythematosus. The bridge of the nose, the cheeks and the auricles had escaped, and there was a large surface of superficial scarring; he thought it very possible that microbic infection was present.

Dr. H. C. SEMON asked how the X-rays were applied; did Dr. Ffrench use a shield? Also, was there any reaction after the small doses of rays in the affected patches?

Dr. J. H. SEQUEIRA (President) said that many dermatologists used X-rays in the treatment of lupus erythematosus in the early days of radiotherapy, but he himself had given up that method because acute reactions were common, and in the cases in which many doses were given grave damage was done. He had followed some cases sufficiently long to see the atrophic skin turn to carcinoma. He was therefore afraid to give X-rays over a long period for any disease whatever. He would like to hear of the later development in the present cases.

Dr. WHITFIELD said that he agreed with the President as to the production of atrophy by long-spaced small doses of the rays, and he (the speaker) suggested that when a physician treated any chronic disease with X-rays he ought to chart his case and keep a record of the amount of rays given; and that in private cases, when the treatment was concluded, he should hand this chart to the patient, so that if another practitioner was consulted he could see what had been done.

Dr. PERNET said he also thought that there was a danger of epithelioma developing when X-rays were administered over long periods of time in such a condition. Pringle had shown a case of epithelioma supervening on lupus erythematosus³ (apart from X-rays).

¹ Pernet, *Brit. Journ. Derm.*, 1907, xix, p. 67.

² Pernet, *Brit. Journ. Derm.*, 1918, xxx, p. 33.

³ Pringle, J. J., *Brit. Journ. Derm.*, 1900, xii, p. 1, with plates and references to other cases.

42 Sequeira: *Tuberculosis Cavi Nasi*; Dowling: *Erythrodermia*

Dr. FFRENCH (in reply) said that Dr. Adamson had confirmed the diagnosis in these cases. He (Dr. Ffrench) did not think that the patches seen on the face, and referred to by Dr. Vinrace, had been caused by the CO₂. There had been very slight reaction after the application of the rays. No aluminium shield had been used; the rays had been given without filtration. He did not think smaller doses had been successful.

An Unusual Case of Tuberculosis Cavi Nasi.

By J. H. SEQUEIRA, M.D. (President).

THIS patient is a married woman, aged 56, and she came to my out-patient department with a large, broad swelling at the root of the nose. In the centre of the swelling there was an ulcer, from which came a sanious discharge. Fifteen years ago the patient received a severe blow on the nose. There was a history of a miscarriage, and of a premature birth. The condition simulated a gummatous infiltration with ulceration. Syphilis was excluded by the fact that the patient has had the trouble fifteen years, and that the Wassermann reaction is negative. I sent the patient to Mr. Norman Patterson, who examined the interior of the nose, and found a polypoid mass. He curetted a large amount of the material away and had it examined, and tubercle bacilli were found in these scrapings. It would be reasonable, following French usage, to describe the condition as a tuberculous gumma. Mr. Patterson proposes to remove as much of the diseased area as possible, and small doses of tuberculin will be administered.

Congenital Ichthyosiform Erythrodermia.

By G. B. DOWLING, M.D.

THE patient, aged 54, has had the condition from birth. Practically the whole of the surface is covered with large polygonal thick scales, in colour ranging from silvery white to brownish or even black. These are particularly large and thick on the back, thighs and legs. There are also some thick hyperkeratotic masses in the flexures.

The scales can be detached in one piece by pulling, and some desquamation takes place from friction. The skin beneath is universally red and is retracted, so that the limbs are somewhat wasted and the face drawn.

There is marked ectropion, the eyelashes pointing vertically upwards and downwards. The palms show the changes characteristic of hereditary tylosis, a point which, as Dr. Adamson to-day pointed out to me, serves to distinguish this condition from true ichthyosis in which one invariably finds accentuation of the normal epidermal creases. This case is one of ichthyosiform hyperkeratosis or congenital ichthyosiform erythrodermia. To the same group belongs the condition of foetal ichthyosis or "harlequin foetus." They belong to the naevi group, and I think are unrelated to ordinary ichthyosis.

Discussion.—Dr. J. H. SEQUEIRA (President) asked whether there were any blisters —(Dr. DOWLING: I do not know)—because cases had been shown in which tylosis associated with the condition was almost indistinguishable in parts from epidermolysis bullosa.

Dr. BARBER asked whether Members had carried out the Wassermann test in these cases. He agreed that the condition was quite different from ordinary ichthyosis: one point of distinction was the involvement of the palms of the hands in ichthyosis, and another was that the skin in the joint flexures, except in very bad cases, was almost normal. In these ichthyosiform nevi, however, the flexures were, if anything, more affected than the rest of the skin. A child with this condition in his (Dr. Barber's) ward had been found to have a strongly positive Wassermann reaction. Antisyphilitic treatment had had a remarkably good effect on the skin. For a time no local treatment had been given; she had had injections of bismuth, and mercury and iodide had been given by the mouth.

Dr. PARKES WEBER commented on the striking chronic retraction of the skin of this patient's face, and asked if this had been noted in other cases of the kind.

Dr. S. E. DORE said that he had three cases of this condition in one family under his care, and in all three the patients had retraction of the eyelids. He would have a Wassermann test carried out, but he had no reason to think the cases were syphilitic.

Dr. A. M. H. GRAY said that he had at present under his care a child who had a zoniform *nævus*, and bullæ had developed in the flexures of the wrists and the axillary regions, where the lesions were most strongly marked.

Case of Tinea of all the Nails in a Child.

By W. F. CASTLE, D.S.C., M.D.

THE patient, a boy, aged 5½, is suffering from an affection of all the nails of the hands and feet. The trouble started in the thumb nail of the right hand six months ago and rapidly spread to all the nails of both hands. The feet were affected shortly afterwards. The nails are brittle and show great thickening and heaping up of the nail substance, while the peri-onychia tissues show a considerable degree of inflammation. The nails can, in most cases, be removed quite easily and painlessly with forceps. The tinea was cultured on Sabouraud's medium, and cultures and subcultures are shown. A section of the nail, showing spores in the matrix, was prepared for me by Dr. Canti and is shown under one of the microscopes. The child's general health is excellent: his brother, aged 7, is not affected.

Discussion.—Dr. W. JENKINS OLIVER said that in his opinion the culture shown might well be that of a trichophyton.

Dr. PERNET said he considered that this case did not fit in with a diagnosis of tinea of the nails. He (the speaker) could not see any trace of fungus in the section of the nail, in the part pointed out to him by Dr. Castle. He thought it was more likely to be a syphilitic condition of the nails.

Impetigo with Hypertrophic Scar Formation.

By W. F. CASTLE, D.S.C., M.D.

THIS patient, a male infant, aged 6 months, is shown because of the hypertrophic scar formation following on an apparently typical impetigo. The history is that he had a generalized bullous eruption on the third day after birth, and that since then scattered patches of impetigo have appeared from time to time all over the body, especially in the groins and down the back of the legs, in both of which places hypertrophic scars may be seen. The scar on the back of the right leg extends from the buttock to the heel, and although it is disappearing in places, it still somewhat resembles a linear *nævus*. Two isolated patches have appeared during the past week, one on the sole of the right foot and one over the external malleolus.

Discussion.—Dr. DOWLING said that he thought this was lichen planus hypertrophicus developing upon a scar. There were also some quite fresh violaceous papules developing spontaneously on the limbs, in places which apparently had not been the seat of any previous lesions.

Dr. J. H. SEQUEIRA (President) said that he was inclined to regard this condition as an eruption caused by bromide, in spite of the absence of history.

Multiple Subcutaneous and Cutaneous Tumours. ? (Parosteal) Chondromata.

By W. JENKINS OLIVER, B.M.

THESE tumours and nodules vary in size from that of a pea to that of a pigeon's egg, and are arranged in groups, mainly about the elbows, knees, left ulnar border, left wrist and left little finger. The patient, a man, aged 20, noticed the first nodule on the left chin about five to six years ago, while all the remaining tumours appeared in the course of the subsequent twelve months, except one about the right elbow which was the last lesion to appear (some three years ago). According to the patient's own statement the present condition has persisted for four years, none of the tumours appearing to alter in character or size until six weeks ago, when he knocked the left wrist, causing softening of one of the tumours and discharge of the chalky material which it contained. The "lumps" had never been painful or tender. There is no original traumatic history. The patient is in good health otherwise, is maintaining his weight, and denies having had any venereal disease; the Wassermann reaction is negative. He has always lived in the United Kingdom and has never been in any tropical countries. There is no history of any similar lesions occurring in his family: no tuberculosis.



FIG. 1.—Right elbow.

The majority of the lesions are firm and hard; a few are softer: two large tumours on the ulnar side of the left wrist show fluctuation. They do not appear to be attached to any underlying bone and many are definitely connected with the skin. Careful palpation over the dorsal aspect of the wrist shows that one small nodule moves with the extensor tendon.

Examination of the material from the upper fluctuating tumour about the wrist revealed a white amorphous substance insoluble in acid and ether, containing no cells or organisms (bacterial or fungoid). I hope to obtain a report on the chemical nature of this substance. Radiologically there are definite shadows, with clear, regular outlines quite distinct and separate from the bones, corresponding to the sites of the tumours. A radiogram of the left leg shows an almost continuous plate-like shadow about the lower half of the shin distinct from the tibia and fibula. Section

of one nodule removed from the right thigh (quadriceps extensor tendon region) suggests a new growth with the appearance of an encapsulated fibro-chondroma with calcification, without any sign of bone formation.

Discussion.—Dr. PARKES WEBER said he regarded this as a magnificent example of multiple calcification of unknown origin in the subcutaneous tissue and the deeper layers of

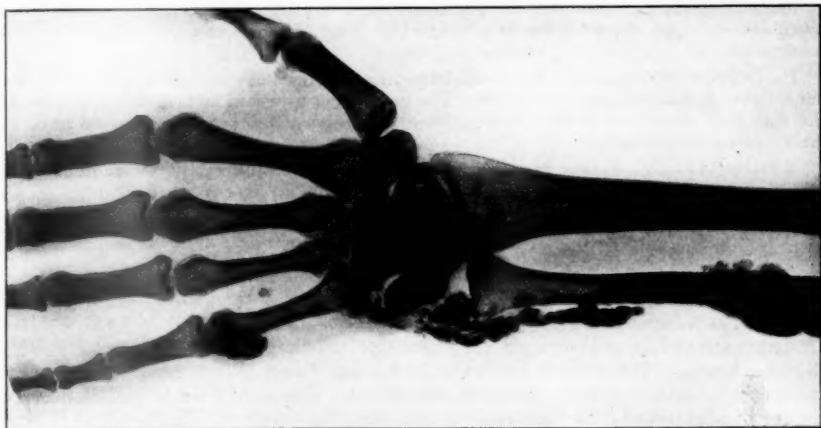


FIG. 2.—Hand and wrist.



FIG. 3.—Left forearm.

the dermis. This condition had been called "Kalk-gicht" (chalk gout); he would prefer to translate the term into English as "calcareous gout." The condition (or a variety of it) was first described in Switzerland by H. Weber,¹ and since then many other descriptions² had

¹ H. Weber, *Correspondenzbl. f. Schweiz. Aerzte*, Basel, 1878, viii, p. 623.

² See references given by F. P. Weber, "Subcutaneous Calcinosis," *Trans. Seventeenth Internat. Congress of Med. (Dermatology)*, London, 1913, p. 179; also *Urolog. and Cutan. Review*, St. Louis, 1923, xxvii, p. 409.

been published. In the present case, unfortunately, there had been no chemical analysis made of the calcareous material; it would be interesting to know whether it consisted chiefly of calcium phosphate or calcium carbonate. In France, great stress had been laid on calcium phosphate in such concretions (so-called Profichet's disease). Of the greatest interest in this case was the discovery of cartilage by microscopical examination of one of the calcareous concretions; that ought to be confirmed. Even if it were confirmed, it was likely that the formation of cartilage or bone was secondary. Almost anywhere in the body where there were calcareous deposits, even in old calcareous tuberculous lesions in the lungs, the formation of true bone might occur in the long run, which could be demonstrated by microscopical examination.

Dr. OLIVER (in reply) said he would have imagined calcium carbonate to be soluble in acids, but this material was not soluble. The pathologist to whom he had shown the section had said that there was no evidence of bone formation. He (Dr. Oliver) would have the chalky material investigated.

Postscript.—Dr. J. R. Marrack reports that the chalky material consists of calcium phosphate and calcium carbonate. There is no excess of cholesterol in the blood, while the content of calcium in the serum is rather below the normal figure.

Case of *Acne Agminata*.

By H. C. SEMON, M.D.

THE patient is a widow, aged 37. She has two healthy children, aged 10½ and 13 respectively. There have been no miscarriages and the Wassermann reaction is negative. She has had a thyroid enlargement (adenoma) since childhood. No history of adenitis or other tuberculous manifestation could be obtained.

In October, 1925, she first noticed the gradual appearance of painless non-irritable spots on the upper lip, to the outer side of the right ala nasi. She came to the hospital in November. The lesions consisted then, as now, of raised, reddish-brown, waxy papules about the size of a hemp seed. They are grouped in clusters of six to twelve on the chin, cheeks and scalp. There is no tendency to necrosis or suppuration. Diascopy reveals a very definite fawn-coloured infiltration. No scars are present. Adenoma of the sebaceous glands was suspected, but before excision of a papule for histological examination, the patient was seen by Dr. Gray, who kindly sent me a considered opinion that this was probably a case of so-called acne agminata or folliculitis, of tuberculous ætiology, and allied to the papulo-necrotic group of tuberculides. The histological findings amply confirm this view, as can be seen in the slide submitted to-day. There is round-celled infiltration in the cutis, with several tubercles containing giant cells, and lymphoid- with a few mast-cells. Light treatment combined with sodium morrhuate injections has effected a distinct improvement.

Discussion.—Dr. A. M. H. GRAY said that he did not think there was any doubt that this was a case of acne agminata, and he thought it identical with cases which Barthelémy had described as acnitis. He (Dr. Gray) did not regard these cases as papulo-necrotic tuberculides, but as belonging to the group of Boeck's sarcoids. That was why he was anxious to have the extremities X-rayed and the tuberculin reaction done. With regard to treatment, he (the speaker) had recently been trying injections of sodium morrhuate in lupus pernio and in Boeck's sarcoid. In view of Sir Leonard Rogers' work he wished to see the effect on skin lesions which were supposed to be due to the tubercle bacillus. He had treated a series of cases of lupus vulgaris, of lupus erythematosus, and one or two known tuberculides, such as Bazin's disease, also two cases belonging to the benign lympho-granulomatous group. The effect on lupus vulgaris and lupus erythematosus had been very slight; the improvement which resulted in some cases might have occurred from other causes. But the effect on the first case of sarcoid was extraordinary; this case had been treated with salvarsan and many other remedies, with only slight transitory effect, but half a dozen injections of sodium morrhuate cleared up all the patient's lesions and the patient had remained well. He (Dr. Gray)

had now under treatment an extensive case of lupus pernio, and that was also responding well to the treatment. He was very anxious that the treatment should be tried for acne agminata, because he thought it might help to settle the nature of the condition. He hoped Members who tried it in these cases would report their results.

Dr. PERNET said that in 1902¹ he had shown sections from Radcliffe-Crocker's case of acne agminata depicted in his third edition,² and had demonstrated that the lesions were due to disorganization and destruction about the sweat-coils. No plasma cells had been present. There had been no evidence of tuberculosis, and staining for tubercle bacilli had proved negative.

Unusual Case of Melanotic Nævi.

By H. C. SEMON, M.D.

THIS child, aged 5½, has a large number of intensely pigmented flat and verrucose nævi on the trunk. The largest measures about 3½ inches in diameter, but there are many intermediate sizes, and pin-point black specks which appear to be grouped as satellites round the larger nævi. On the flexor aspects of both forearms there are numerous non-pigmented, raised, soft nævi, which, in places, resemble the lesions of xanthoma nodulata. The mother states that these were not present at birth, and are believed to be increasing in size and number. My chief object in presenting this case is to obtain the views of Members as to whether any useful purpose would be served by excising or otherwise destroying the larger melanotic verrucose lesions on the trunk, on the ground of possible malignant degeneration in later life.

Discussion.—Dr. S. E. DORE said he thought that if the pigmented nævi were very numerous, they should be left alone and not excised, unless they were situated on the face, when electrolysis or excision might be resorted to.

Dr. J. H. SEQUEIRA (President) said that pigmented moles were very common, while melanotic sarcoma was comparatively rare. The majority of pigmented moles did not become malignant.

Report on a Case of Dermatitis Artefacta.³

By S. E. DORE, M.D.

PATIENT, a girl, aged 19, has been under my care for five months, with linear excoriations on the arms. One arm was put up in plaster, and the lesions then appeared on the other arm, and when an occlusive dressing was put on this arm, lesions appeared on the skin above and below the dressing. The point I wish to emphasize is that I sent the patient to Dr. Stoddart, at St. Thomas's Hospital, and he said that the case was one of dual personality, and that the patient was unaware that she produced the lesions herself. Dr. Pernet had mentioned the association of dual personality and artefact, but this is the first case which I have seen in which the diagnosis has been definitely made by an alienist.

Discussion.—Dr. J. H. SEQUEIRA (President) said that many cases of the kind showed mental stigmata, and possibly medical men were a little too severe in such cases when they expressed disbelief in the patient's statements. He (the President) had had one patient who

¹ Pernet, *Brit. Journ. Derm.*, 1902, xiv, p. 131.

² Radcliffe-Crocker, "Diseases of the Skin," vol. ii, p. 1096, fig. 70.

³ Dr. Dore said that he had the President's permission to make some remarks about this case, which was shown, but not discussed, at the last Meeting.

had produced very deep lesions, and who was very indignant when charged with so doing. Another patient had been admitted into hospital supposed to be suffering from "acute abdomen," and it had been discovered that she had pushed needles into her umbilicus. He (Dr. Sequeira) frequently raised the question in his department as to whether such cases should not be sent to the mental specialist rather than to the dermatologist.



Dr. PARKES WEBER said he agreed that it was most important to settle the question as to whether a dual personality was sometimes the psychical explanation of such cases. Such an explanation would account for the fact that occasionally not only the patient's relatives but even the family doctor were convinced that the patient was speaking the truth.

Section of Dermatology.

President—Dr. J. H. SEQUEIRA.

CASES.

Xanthoma Tuberosum Multiplex.

By S. E. DORE, M.D., and O. L. V. DE WESSELOW, M.B.

I—Dr. S. E. DORE.

PATIENT, female, aged 31. Nothing of importance in family history.

History of Present Complaint.—In good health until November, 1923. From this date until April, 1924, complained of intermittent attacks of abdominal pain. In April, 1924, became jaundiced, the pain continuing.

The cutaneous lesions appeared six months ago, first on the fingers, then on the arms, face, legs and trunk. There was no history of cholelithiasis. Urine contained a trace of urobilin, but no bile pigment.

Admitted to hospital April, 1924. Marked jaundice, liver and spleen just palpable; no other physical signs. The attacks of pain continued, beginning in the left hypochondrium and radiating towards the left shoulder. They were paroxysmal in character and accompanied by profuse sweating.

Exploratory operation, October, 1924. No gall-stones found in gall-bladder or ducts. Liver soft and enlarged to 2 in. below the costal margin. Slight pyloric hypertrophy. Appendicectomy performed, as appendix showed slight fibrosis.

Subsequent History.—Jaundice more pronounced. Sent to me by Dr. de Wesselow in February, 1925, for opinion on cutaneous lesions. Blood shows high degree of hypercholesterinæmia.

Present Condition.—Xanthomatous infiltration present in linear, nodular and plane varieties, but mainly of linear type, occupying folds of nearly all the flexures in body. Xanthomatous tracts especially marked in anterior axillary folds, the creases of the elbows and wrists, and especially those of the palms and flexures of the fingers. The inguinal, gluteal and anal folds are similarly affected, and also those in the neck. Small nodules are interspersed with the linear lesions on the arms, elbows and knees, in the neighbourhood of the tendo Achillis, and on both sides of the dorsal surfaces of the feet; there are also a few in the operation scar. On the face the inner canthi and eyelids are profusely infiltrated with xanthomatous deposit in plaques and small nodules. There is marked, but not very deep, jaundice of the face and conjunctivæ.

II—Dr. O. L. V. DE WESSELOW.

I have certain chemical findings in the case to report. The cholesterol content of the plasma amounted to 1,325 mgm. per 100 c.c. The lævulose test of hepatic function gave no evidence of any general damage to the hepatic parenchyma. The blood-sugar, three hours after a meal, was 0.120 per cent., and the urine was free from sugar and ketone bodies. There is therefore no evidence that in this patient the disease is associated with diabetes mellitus, as in many of the reported cases. The Van den Bergh reaction gave a very delayed direct response, no colour appearing for six minutes; the indirect strongly positive; quantitative 2.8 units. The urine showed bile-pigment, and a positive urobilinogen reaction in a dilution of 1 in 50. The striking feature of the case is the great excess of cholesterol in the blood. Harrison has recorded a figure of 640 mgm., and in three cases examined by Major

the plasma cholesterol varied from 432 to 632 mgm. Major has also quoted cases from the literature in which the plasma cholesterol had reached a figure as high as 1,260 mgm.

It seems reasonable to attribute the excess of cholesterol in the blood of the present patient to biliary obstruction, since such obstruction is known to produce hypercholesterinaemia. Against that view is the equivocal Van den Bergh reaction, the prompt direct reaction, characteristic of obstructive jaundice, being absent.

Discussion.—Dr. DOUGLAS HEATH said that two years ago he had had a case similar to this, showing infiltration of the skin with xanthoma nodules. In that case there had been an extensive sheet-like induration over the shoulders. The urine was loaded with bile, and during the whole time the motions were putty-like.

His (the speaker's) reason for mentioning that case was because he believed the prognosis in this condition to be very bad. In his case an operation had been performed because it was hoped that gall-stones would be found, the view having been expressed that the common bile-duct was blocked. The patients in these cases were generally supposed to live about twelve months after the obstruction of the duct had taken place. The patient in his case had lived for eighteen months afterwards. With regard to the case now shown, although there were not at present any signs of serious illness, he (Dr. Heath) would take a grave view. It might be well to call in surgical aid.

Dr. F. PARKES WEBER said that a difficult question in regard to the case was whether another exploratory operation should be advised in order to ascertain the cause of the chronic jaundice. Any extensive abdominal operation would be dangerous in a case of the kind, and the patient might probably live for years if left with her jaundice. The absence of any obvious enlargement of the liver might be explained by the incompleteness of the biliary obstruction, the urobilinogen in the urine showing that some bile was entering the duodenum. In two recent necropsies at the German Hospital on cases of chronic jaundice due to practically complete obstruction in the extrahepatic bile-ducts (primary adeno-carcinoma of the duct), the liver was enlarged owing to distension of all the intrahepatic bile-ducts with colourless bile. In the present case there was just the possibility of a xanthomatous change having developed in the bile-ducts as a sequel to preceding cholelithiasis.

Gaucher's Disease with Cutaneous Lesions.

By S. E. DORE, M.D.

THIS patient is a woman, aged 27. She was in good health until 1921, when she had a stillborn child. Afterwards she became weak and anæmic, and complained of dyspnoea and anorexia. She had a persistent vaginal discharge, accompanied by a dull aching pain in the abdomen. She was admitted to the hospital on April 14, 1924, suffering from anæmia and abdominal pain. Splenectomy was performed in June, 1924, by Mr. Percy Sargent, to whom I am indebted for permission to bring her here. The cutaneous lesions, which appeared in April, 1925,—that is, nine months after the operation—consisted of small, raised, brown nodules on the arms, and a large patch-like lupus on the nose. She has been having ultra-violet light treatment, and they have now nearly disappeared. An interesting question is whether there is any connexion between the cutaneous lesions and Gaucher's splenomegaly. I had the advantage of Dr. Parkes Weber's opinion on this point, and his view was that although the section of the spleen showed typical Gaucher's cells, these were not present in the section of the cutaneous nodule, and he regarded the two conditions as independent.

When the case was sent me for an opinion I suggested the diagnosis of multiple benign sarcoid, and the pathological report of a biopsy was that: "The section showed numerous large areas with endothelial cells, with giant-cell formation not related to lymphadenoma, but possibly to Gaucher's disease."

Radiograms of the hands showed no bone changes. The patient refused to have a tuberculin test done, and it has not been possible to investigate the tonsils, but Schaumann's benign lympho-granuloma can probably be excluded. The sections of the lesions on the skin, as well as their clinical appearance, seem to confirm the diagnosis of Boeck's cutaneous benign sarcoid.



Gaucher's disease with cutaneous lesions (? multiple benign sarcoid).

Discussion.—Dr. ARTHUR WHITFIELD said he thought that so far as the arrangement went the section shown by Dr. Dore was very suggestive of Schaumann's benign lympho-granulomatosis. On the other hand the cells constituting the infiltration seemed to be nearly all well-developed fibroblasts, with darkly staining nuclei, in marked distinction from the very pale staining cells in Schaumann's disease. For this reason, when discussing the case privately with Dr. Dore he (the speaker) had taken the view that it was not Schaumann's disease. On thinking the matter over, however, he had remembered that all the sections he had seen previously had been taken from lesions exhibiting the disease in full activity. Owing to efficient treatment this patient had almost recovered and the section was taken while the disease was in retrogression. He (Dr. Whitfield) imagined that in this stage the infiltration would be likely to show active, well-formed fibroblasts and therefore this distinction between the two varieties of cell might be fallacious.

Dr. F. PARKES WEBER suggested (as Dr. Whitfield had done) that the cutaneous lesion might have been in process of involution when the microscopical sections were made, and that this fact might account for the absence of the "large clear cells" characteristic of the disease termed "lymphogranulomatosis benigna" by Schaumann. There was no evidence at

present that the large clear cells in the lesions of lymphogranulomatosis benigna were identical with the "large clear cells" of Gaucher's disease, but he believed that lesions from the two diseases had not as yet ever been examined and compared by the same pathologist.

Dr. J. H. SEQUEIRA (President) said that in this case there were two conditions; Gaucher's disease and lympho-granulomatosis.

Nodular Leprosy previously shown.

By S. E. DORE, M.D.

I SHOWED this patient here in October, 1924.¹ He was born in this country, and contracted the disease from his father who developed leprosy fourteen years after coming here from India. When I first saw the boy he had had nodular leprosy for eighteen months. The disease has steadily progressed and I cannot say that treatment has done him any good at all. He has had injections of E.C.C.O. and mugrol and sodium gynocardate pills. I could not increase the injections of E.C.C.O. because they made him ill, and he could not take chaulmoogra oil. A vaccine was prepared from a nodule, but this only lasted three months, and I do not think there was any benefit.

I have brought him in order to show the rapid progress that the disease has made in two years and the failure of the treatment to check it. He has also had some light baths and X-rays, but I have not been able to give him intravenous injections of sodium gynocardate as his mother will not let him come into the hospital.

Discussion.—Dr. J. H. SEQUEIRA (President) said the Members would recollect that Dr. Lancashire had had an unpleasant experience with intravenous injections of E.C.C.O., but had obtained an apparent cure by giving the combination intramuscularly.

Dr. ARTHUR WHITFIELD said he thought the Section should make a protest against the erroneous statements made to the public regarding "cures" for leprosy. It was scarcely possible to take up an evening paper without seeing a report of a lecture or article giving the impression that leprosy had been deprived of its terrors. Dr. Dore's experience in the present case, and Dr. McLeod's experience in other cases, was that such was not a fact. The treatment of leprosy had not been fundamentally advanced during the last fifty years, and the actual state of affairs should be widely published, to counteract the unfortunate misinformation. He (the speaker) did not think any real cure for leprosy had been found; some patients had been benefited, some had not, and some tended to recover spontaneously.

Dr. G. PERNET said that when Dr. Dore had first shown this case he (the speaker) had said that he regarded the prognosis as rather a bad one, because of the patient's youth.

Dr. A. M. H. GRAY said that when first this patient had been shown, he (Dr. Gray) had quoted the case of a boy who had improved considerably under treatment by intravenous injections—instead of intramuscular injections—of gynocardate of soda, the tumours on the face going down, and the pain which he had been having in his feet becoming less. But the time came when no further intravenous injections could be given owing to the difficulty of finding veins, and he was put on to E.C.C.O. and kept on it for two years. There was no doubt that he had relapsed severely; his face was now as bad as when he had first been seen. He (Dr. Gray) had resumed treatment by intravenous injections in this case two months ago, but there was no marked improvement. The patient was now about seventeen years of age.

Dr. J. H. SEQUEIRA (President) said he thought the condemnation pronounced was too sweeping. He had seen photographs of a large number of cases of this disease which had been treated in the East, and there seemed no doubt that some of the younger patients in leprosy areas abroad had done very well. But as to the permanence of the treatment, he was not prepared to say anything. He, personally, had had extremely good results in a case of nerve leprosy from injections of the type indicated. Whether leprosy, developing in young subjects in this country, was of a more virulent type he did not know.

¹ See *Proceedings*, 1924, xviii, p. 16.



FIG. 1 (a)



FIG. 1 (b)

August 12, 1924.

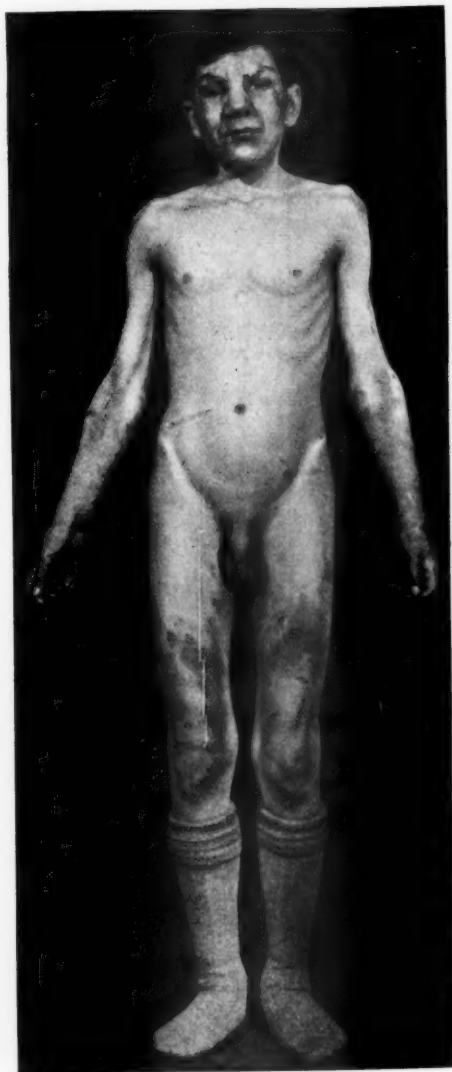


FIG. 2.—December 11, 1925.

Dr. J. M. H. MACLEOD said that this case was interesting because it was another example of the contraction of the disease by a patient who had never been out of this country; it was the fourth case of the kind to be reported. He (the speaker) had had some experience of injections of sodium gynocardate at the St. Giles' Homes for British Lepers, where a number of preparations of vegetable oils had been used, both by the mouth and by injection, and the conclusion arrived at had been that none of these drugs had so far proved to be specific and curative. Several of the patients were intelligent, took a great deal of interest in their disease, and had strong views and fancies regarding the value of different remedies. Recently they had had an impression that they obtained more benefit from sodium morrhuate.

He (Dr. MacLeod) strongly corroborated Dr. Whitfield's opinion as to the harm done by the publication in the lay press of treatments which were reputed to be "cures" of this disease,

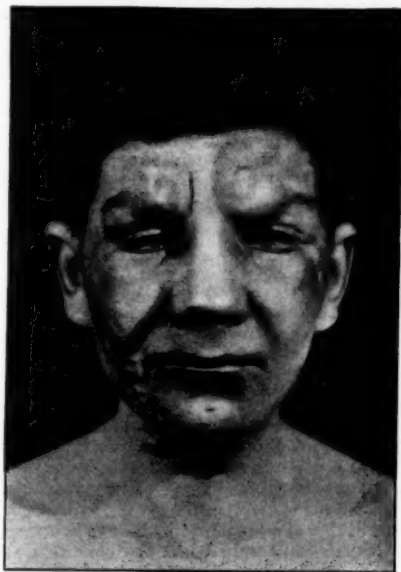


FIG. 3.—February 7, 1925.

but which only caused bitter disappointment to the patients, and were extremely misleading to the public.

Dr. DORE (in reply) said he agreed with the remarks of Dr. Whitfield and Dr. MacLeod. The only case of recovery he had seen was that of a colonel from India, a medical man, who suffered from an old contraction of the fingers of one hand, and who assured the speaker that he had been cured of leprosy and had remained so for many years. Portions of his skin had been excised and microscoped at long intervals, and no bacilli had been found. But he (Dr. Dore) thought that there was a tendency to claim cure prematurely in these cases. A patient with anæsthetic leprosy whom he had shown some time ago at a meeting of this Section was stated to be suffering from trophic lesions resulting from old leprosy, but when he had given her injections she developed a reaction and a macular rash appeared on the body.

Premycotic Erythema.

By J. H. T. DAVIES, M.D.

THIS patient was first seen at the Royal Sussex County Hospital in January, 1926. There had been three or four weeks of severe pruritus in September, followed by a spot on the back, which had since been repeated over the back and chest. There has been no change since January. The eruption consists of macules of crescentic and other shapes, distributed mainly along the lines of cleavage, slightly raised and infiltrated, colour brownish pink; not scaly. Biopsy shows acanthosis, flattening of the papillæ, slight patchy cell infiltration in papillary and deep layers of corium, especially round vessels. The cells are chiefly large round nuclear cells with little cytoplasm, plasma cells nowhere more than three to a field of $\frac{1}{12}$ -in.; here and there giant cells, and normal number of mast cells. A diagnosis of premycotic erythema has been made. With regard to the alternative diagnosis of xantho-erythrodermia perstans, which is reputed to resist any treatment, should I regard the non-disappearance of these lesions after a 1B dose of X-rays as indicative of this condition?

In the event of the diagnosis of mycosis fungoides being confirmed, ought I to radiate the existing eruption, or, bearing in mind the fact that X-rays lose their effect in this disease, to reserve radiation until the tumour stage?

Discussion.—Dr. G. PERNET said that the condition was xantho-erythrodermia perstans, the name he (the speaker) had suggested to the late Dr. Radcliffe-Crocker.¹ Histologically the (Dr. Pernet) had found nothing of any moment.²

Dr. WILFRID FOX said that the way in which the eruption spread diagonally across the body was characteristic. Patients in the cases of xantho-erythrodermia in which he (the speaker) had applied X-rays had been made worse by the treatment, for the eruption spread afterwards to places not previously involved. The condition seemed to be temporarily relieved by the application of beta-naphthol.

Dr. A. WHITFIELD said that he would have thought, except for the fact that there was not any itching, that this was a condition of premycotic erythrodermia; the application of X-rays would be diagnostically conclusive, as under those rays mycosis fungoides would disappear. He (the speaker) was convinced that X-rays constituted the right treatment as soon as that diagnosis had been made. A peculiar reaction had come to his (the speaker's) notice during the treatment of mycosis fungoides by X-rays in a very characteristic case which he had seen in April, 1925. The patient had had the condition all over her head and face, giving her almost the appearance of leonine leprosy; she also had the eruption all over the body and extremities. He (Dr. Whitfield) advised the application of X-rays, warning the friends, however, that the treatment might cause her death. As the natural course of the disease had such terrible results, he (the speaker) had thought the risk justifiable. The patient had been treated by himself (Dr. Whitfield) on two occasions and had, in all, ten pastille doses of the rays, distributed on areas on the head, upper part of the shoulders, and upper part of the chest, a week separating the groups of five. The result was a very severe illness, so that the patient nearly died. But a fortnight after the second group of doses the areas which had been X-rayed began to clear, and without further application of the rays, as she recovered from the profound tissue poisoning. The eruption disappeared from every other area on the body, legs and arms, except one small area at the back of the calf, and a doubtful one on the buttock; these were subsequently X-rayed, and they disappeared too. Unfortunately, however, after she had recovered from the skin condition she became insane, and had remained so, though, physically, she had been quite well and had been heard of since Christmas, 1925.

There was also the question, which he (the speaker) had mentioned some time ago in association with a case of sarcomatosis cutis, that if one X-rayed sufficiently severely, short of burning the patient, so as to concentrate on the original area, the whole disease might be

¹ Radcliffe-Crocker, *Brit. Journ. Derm.*, 1904, xvi, p. 423.

² Pernet, *Brit. Journ. Derm.*, 1904, xvi, p. 457.

cured. That possibility was very convenient in some ways, as one could not apply X-rays directly to certain regions without danger, as for example to the eyelids, without considerable risk to the eyesight. If this patient's insanity was of the toxic variety due to an overdose of X-rays, there was hope for a cure of it. He (Dr. Whitfield) thought it best to apply high doses to one area, and then wait to see whether absorption of the other lesions took place.

Dr. L. SAVATARD said that he himself had had a similar instance, in a case which he had shown at a meeting of the Section some years ago. The condition had cleared up well under X-rays and the areas not subjected to the rays had also participated in the cure, though the dose given was not so large as that which Dr. Whitfield had mentioned. His (Dr. Savatard's) patient had never had more than two pastille doses on the same day.

Dr. S. E. DORE said that in the case of a man admitted to St. Thomas's Hospital in 1903 the diagnosis had been mycosis fungoides. He had had a tumour at the back of the neck, and some plaques on the thighs and legs; these had been treated with X-rays. The patient had come under his (Dr. Dore's) care recently, suffering from typical mycosis which had been rapidly fatal, but he had apparently been free from lesions for nearly twenty-three years.

Dr. WHITFIELD said that permanent cure was occasionally obtained. He had once had a patient aged 55, whose condition was diagnosed as mycosis fungoides. He was seen by Dr. Colecott Fox, who had agreed with this diagnosis, which was confirmed by a biopsy. X-rays had been applied, and the condition had cleared up entirely, though only one series was given. The patient had died of apoplexy when aged over 70. The mycotic lesions had not returned.

Dr. J. H. SEQUEIRA (President) said that some years ago he had shown two cases of the condition at a meeting of the Section. In one there had been a general erythrodermia with multiple mycosis fungoides tumours. These had cleared up temporarily under X-rays, but ultimately the patient had died. In the other case there had been a large reniform mycosis fungoides tumour, which had cleared up under X-rays. He (the President) had lost sight of that patient for ten years, but he believed he would have come back to him if there had been any return of the condition. There had been no recurrence during the five years the patient was under observation, though there had been an atrophic scar with telangiectasis.

Postscript.—Since the meeting, one area of the eruption has received a 1B dose without disappearance of the lesions after sixteen days.

Multiple Basal-celled Carcinoma.

By LOUIS SAVATARD.

THIS patient first came to hospital twenty years ago. She was then under X-ray treatment for rodent ulcer on the left side of the forehead, and there are now several carcinomata, of superficial type, scattered over the forehead, behind the ears, and on the back. I show it in conjunction with a slide from a case of pre-cancerous dermatosis (Bowen). Dr. Barber showed a section at the last meeting of what he considered to be Bowen's pre-cancerous dermatosis,¹—a diagnosis with which I disagreed. I bring this section and case to-day to demonstrate that there is a difference between Bowen's pre-cancerous dermatosis and these superficial rodent ulcers, which have been considered and reported from time to time as being cases of Bowen's disease.

Discussion.—Professor R. B. W. WILD said that this patient had been under his (Professor Wild's) care in hospital eighteen years ago and at that time she had had a lesion on the left temple, almost identical with that seen to-day in the middle of her back. The diagnosis eighteen years ago had been non-ulcerated rodent ulcer. She was put under short sittings for X-ray treatment once a week, and, as could be seen by the scar on the temple, the result had been very satisfactory. At that time she had had no other lesions at all. It was now of considerable interest to him (the speaker) to see the development of lesions of similar type on other parts of the body after so long an interval.

¹ *Proceedings*, 1926, xix, p. 37.

58 Graham Little: *Lichen Plano-Pilaris*; *Lichen Planus of Penis*

Dr. J. H. SEQUEIRA (President) said that he had been asked by Dr. Lieven, of Aix-la-Chapelle, to say that in abstracting the reports of the meeting of this Section he (Dr. Lieven) had been struck by the number of cases of multiple basal-celled carcinomata reported. Apparently the disease was rare in Germany.

Lichen Plano-Pilaris.

By E. G. GRAHAM LITTLE, M.D.

PATIENT, a female, aged 45, showing patches of typical lichen planus in the groin and on the thighs, together with lesions upon the upper and anterior aspect of the arms and also upon the back, closely resembling lichen spinulosus and grouped like that disease.

This type, called by Pringle "lichen plano-pilaris," is of considerable rarity and is of special interest in connexion with the view expressed by some observers that lichen spinulosus is, in fact, a form of lichen planus.

Sarcoid.

By E. G. GRAHAM LITTLE, M.D.

PATIENT, a female, aged 39, showing a plaque of localized induration (about the size of a two-shilling piece) over the chin. This had persisted for over twelve months. X-ray photographs showed no changes in the bones of the fingers or toes.

Dr. J. H. SEQUEIRA (President) said that it was difficult to make the diagnosis of sarcoid simply on the appearance. Radiograms of the bones were negative, but he (the speaker) believed that a microscopical examination had not been made.

Lichen Planus of Penis, Scrotum and Scalp.

By E. G. GRAHAM LITTLE, M.D.

PATIENT, a male, aged 39. The lesions have a most unusual distribution. There are typical lichen planus patches on the glans penis and on the scrotum, and there is a patch of the disease on the scalp. The eruption commenced three years ago upon the scrotum. There is no involvement of the mucosa.

Discussion.—Dr. J. H. SEQUEIRA (President) said that a paper had been recently sent to him (the speaker) by Dr. Pautrier, in which the author stated that he had been able to cure lichen planus, not only of the skin, but also of the mucous membranes, by irradiation of the spinal marrow, three to five units being given, without any other treatment whatever, either local or general, and asked whether any member of the Section had tried this treatment. He (Dr. Sequeira) intended to try it at an early opportunity, after this very definite statement by a practical observer.

Dr. DOUGLAS HEATH said that the condition was here seen in a very late stage, and lichenification of that kind might be left after other affections. He (the speaker) did not regard the scalp patch as suggestive; there was not the raised disc on which Dr. Whitfield laid so much stress, and perhaps the patient had a very seborrhœic head. The mid-line of the scrotum was affected and fissured. Lichen planus was a disease in which there was an increase of substance, and in which fissuring was uncommon. The condition on the penis and scrotum would, he (Dr. Heath) thought, be found in a very late eczematoid condition. Of course, the characteristic signs of lichen planus might have now disappeared.

Section of Dermatology.

President—Dr. J. H. SEQUEIRA.

Premycotic Stage of Mycosis Fungoides.

By S. HARDY KINGSTON, M.B., Ch.B., D.P.H.

PATIENT, a man aged 55. Ten years ago a patch of so-called "eczema" first appeared on inside of right thigh. Irritation always severe. Since then this area has enlarged to twice its original size. In addition, many other lesions have appeared on the chest, arms and legs. The plaques were red, dry, scaling, infiltrated, and of irregular shape and size. Islands of healthy skin appeared in between these lesions. Glands in axillæ are enlarged. Spleen, hair and nails not affected. Blood-count normal. The disease proved rebellious to all forms of local treatment except electric light bath treatment, used before coming under my care. X-rays caused a regression of symptoms. But the condition has now relapsed.

Section shows some diminution of stratum granulosum and occasional parakeratosis in epidermis; dense, well-defined cellular infiltration of subpapillary layer of dermis. The cells are of small round and spindle type, with an occasional multinucleated cell. Plasma cells and eosinophil leucocytes are present in small numbers and there is a slight increase of mast cells.

Dr. W. KNOWSLEY SIBLEY said that he himself had tried ultra-violet light for a similar condition, but had found it of very little use. A woman had been attending the hospital for many years, and had had so much X-ray treatment that he (the speaker) was almost afraid of giving her any more, therefore ultra-violet light was tried, but he had been so far unable to attribute any improvement to that method.

Case for Diagnosis (Chronic Symmetrical Granuloma of the Extremities resembling Sarcoid (Schaumann)).

By H. C. SEMON, M.D.

PATIENT, a tailor, aged 55. He first noticed the eruption as a small reddish patch, on the back of the left hand, in the summer of 1913. There was no itching or other symptom associated with it. Gradually it enlarged, and other similar patches appeared on the back of the right hand, on the shins, and on the insteps. A patch on the left side of the face developed in 1922.

Physical Signs.—The lesions consist of smooth, symmetrical, reddish-brown infiltrations, without any tendency to ulcerate or even to scale. On diascopy a brownish stain is apparent. There is no tendency to the formation of tumours, and no suggestion of purpuric extravasation. The lesion on the cheek is slightly nodular in its lower extremity, and the margin is less definitely sharp than that of the lesions on the backs of the hands and fronts of the shins, in which latter situation, doubtless because of the venous stasis, the colour is purple or bluish rather than reddish-brown. None of the lesions exhibit scarring or atrophic tendency, and the patient is very definite in his statement that at no time have there been any subjective manifestations.

There is no anæsthesia of any patch, and the bacillus of leprosy could not be demonstrated either in the section from a patch on the forearm, or in the mucus from the nasal passages.

60 Semon: *Chronic Symmetrical Granuloma of the Extremities*

Dr. Ernest Shaw, Pathologist, Royal Northern Hospital, has kindly reported on the section:—

"Beneath the epidermis, which is normal, a clear hyaline layer runs along the whole length of the section. Below this are large collections of small, round inflammatory cells, among which there are numerous larger mononuclear (plasma) cells . . . A section stained with methylene blue reveals numerous large cells filled with blue granules and a nucleus is partly visible in some of them. The cells are variable in shape, some spindle, others long and thin, and others branched. They lie in the fibrous tissue and among the small round cells. These cells are apparently fibroblasts (mast variety)."

The patient's general health is very good, and he only seeks advice for the eruption because employers object to its appearance, and he can get no work. He has never been seriously ill, and has never been out of the country. The Wassermann reaction is negative; there is no history of syphilis or glandular enlargement at any time of his life. There is no history of tuberculosis in the family. A blood-count reveals no abnormality. X-ray photographs of the chest reported on by Dr. Goulesborough are normal, and there is no deposit to be seen in the phalanges. Further evidence against the possibility of a sarcoid (Schaumann type) is the fact that von Pirquet's reaction is very strongly positive. The report on the section does not help the diagnosis very much, but so far as it goes, and on the appearance of the lesions and their extreme chronicity, it would seem to favour the view that we have to deal with a chronic granuloma, probably of tuberculous origin. The fact that there has been distinct fading and flattening of patches since ultra-violet therapy was begun, some three months ago, seems to support the suggestion.¹

Discussion.—Dr. WILFRID FOX said he thought the microscope helped in the diagnosis. If this slide alone were shown one would diagnose it as a chronic syphilide; there were plasma cells, and they were collected where they should be, around the vessels in the subpapillary plexus. He thought that the microscopical appearances were so typical that greater importance should be attached to them than to the negative Wassermann reaction.

Dr. A. WHITFIELD said he hesitated to make a firm diagnosis, but when he saw the case he suggested to Dr. Semon that it belonged to the group of lupus erythematosus. It was similar to one which Dr. Radcliffe Crocker showed to the Dermatological Society of London under the name "nodular lupus erythematosus." If this were so, it belonged to the type in which the persistent erythema was very marked, and the changes of a secondary nature in the epidermis were slight. He did not think that the microscopical appearances were conclusive, but they were consistent with the diagnosis of lupus erythematosus. There was enormous œdema, and beneath it a narrow sheet of infiltration, which, though not diagnostic, was found in lupus erythematosus, and the negative Wassermann and positive von Pirquet reactions were also consistent with such a diagnosis.

[Dr. SEMON promised to report further progress.]

" Reticulated Pigmentary Poikiloderma of the Face and Neck " (Civatte).

By H. W. BARBER, M.B.

In the *Annales de Dermatologie et de Syphiligraphie*, October, 1923, appeared an article by A. Civatte, in which he described three cases of a condition which he named "Poikilodermie réticulée pigmentaire du visage et du cou;" this he considers to be a distinct clinical entity, not previously defined. On reading Civatte's admirable clinical and histological exposition of his cases, I could not recall ever having seen one, but recently the patient, whom I have shown this afternoon, came

¹ On the possibility of a luetic basis, 5 injections of 0.2 grm. silver salvarsan, with pot. iod. gr. 10 t.d.s. by the mouth, have been given since the case was shown. There has been no appreciable alteration in the appearance of the eruption.

to my out-patient clinic with an eruption which I recognized at once as corresponding exactly to Civatte's description. As far as I know it is the first case of its kind to be described in this country, but perhaps some of the more experienced Members of the Section may recognize the condition under another name.

Mrs. M. B., aged 32, has noticed during the last year or so the gradual appearance on her face of an eruption for which she is unable to account. She cannot exactly date its onset, but states that it appeared symmetrically on the two sides of the face at about the same time, always, however, being more marked on the right side. Her general health is good, apart from some indigestion, with flatulence. She has three healthy children, the youngest being six years of age. Her periods are regular and apparently normal. On ordinary physical examination no signs of organic disease are found. The blood-pressure is 140 systolic, 75 diastolic. A vaginal examination revealed no abnormality of the pelvic organs.

The eruption involves the face only, and is situated symmetrically on either side, being more marked on the right. It occupies an area in front of the ears, extending forwards to the level of the outer border of the eyebrow, downwards to the level of the mouth, and upwards over the forehead. Its morphology is complex, and its characteristics have been defined by Civatte as follows:—

"A pigmented and atrophying erythrodermia arranged in networks; a localized symmetrical eruption practically confined to the face and neck; an evolution more or less indefinite; the dermatosis is seen in women at about the age of the menopause."

On detailed examination of the eruption, as presented in my patient on the right side of the face, there is seen a large, slightly infiltrated, erythematous and pigmented patch with irregular margins, situated over the malar region and temple. The colour of this patch is composite, being a dark reddish-brown, owing to the fusion of the brown of the pigment and the red of the erythema. On the surface are small, white, rather adherent scales, and vitro-pressure reveals a network of very fine telangiectases. As the patch extends upwards on to the forehead the colour changes, the erythema becoming faint, so that brown pigmentation predominates; there is also an irregular brown plaque just in front of the ear, separated from the main patch by white, slightly atrophic skin studded with small points of brown pigmentation, some of which, at least, seem to correspond to the follicles. Just in front of the lobe of the ear is seen an area of superficial atrophy, which is de-pigmented and shows up white in contrast with the normal skin below and the main part of the eruption above.

Histopathology.—In view of Civatte's very complete description of the histopathology of the condition, it was not thought justifiable to make a biopsy on my case. The following is a summary of Civatte's findings:—

A section through an infiltrated erythematous pigmented patch shows:—

Epidermis.—Very little change, except slight hyperkeratosis and swelling of some cells of the germinal layer, which may be separated from neighbouring cells by a few lymphocytes.

Papillary Body.—Diffuse infiltration with lymphocytes and fibroblasts. Beneath the swollen basal cells, above referred to, there is cavitation. In the middle are masses of chromatophores charged with melanin, indicating the pigmentary disturbance. The elastic tissue is strikingly diminished.

Corium.—Situated near the pilosebaceous follicles are lymphoid nodules, lying deeply at a distance from the epidermis. They consist of masses of lymphocytes and mononuclear cells in a delicate reticulum of adenoid tissue. The slight projection of the early lesions above the surface of the skin is largely due to the presence of these nodules.

A section through an atrophic macule shows a general superficial atrophy. *Epidermis:* The thickness of the epidermis is reduced by half, owing to thinning of the mucous body, the horny and granular layers remaining intact. Only a few islets of the germinal layer are left. *Papillary Body:* The papillae and interpapillary projections have disappeared. The infiltration is less, and the chromatophores fewer but still numerous, the pigmentation surviving the early erythema. At the junction of the epidermis and dermis are several hyaline bodies, coloured yellow by van Gieson's stain, pink by eosin, and sometimes brown by acid orcein. The largest are the size of a Malpighian cell or slightly larger. They are often grouped in masses and are always found in the situation of the papillary body. There are also others, much smaller, which lie nearer the epidermis or actually in the lower layers of the mucous body between the epithelial cells. The elastic tissue has entirely disappeared.

62 Barber: *Pigmentary Poikiloderma of Face and Neck; Sarcoid*

Discussion.—Dr. J. H. SEQUEIRA (President) said he took it that Dr. Civatte and Dr. Barber believed this condition to be different from the Jacobi type of case, an instance of which was described by Dr. Rasch in a recent number of the *British Journal of Dermatology*.¹ In those cases, apparently, the eruption was more like a chronic X-ray burn, a telangiectasis with some pigmentation, and was more widely spread.

Dr. J. M. H. MACLEOD said that the atrophy was so slight in this case that obviously the case did not belong to the class described first by Jacobi under the heading of "Poikiloderma atrophicans vascularis," a typical example of which he had seen in 1923 at the annual meeting of the American Dermatological Association.

Dr. A. WHITFIELD said he had seen three cases of the kind, and had regarded them as related to rosacea. Some cases of the latter, instead of attacking the nose, forehead and malar eminences, selected a site in front of the ear and under the angle of the jaw; the latter might be the only area which flushed after meals. The wife of a colleague of his was affected in this way in the latter part of the war; she had been overworked and badly fed, and suffered from severe indigestion. She had a reticular erythematous area over the side of the face which seemed as if it were atrophying, and the condition looked like lichen planus. Neither Dr. Adamson nor himself was happy about the diagnosis. He (Dr. Whitfield) gave her a third of a pastille dose of X-rays every ten days for three doses, but this had no effect. As her general health improved she got rid of the skin trouble, and she had remained free from it for a long time. This present patient said she suffered from appalling headaches and indigestion. He thought the skin condition would disappear as she became cured of her indigestion.

Dr. BARBER (in reply) said that Dr. Rasch's case was complicated by the fact that the patient had undergone X-ray treatment, and he gathered that Dr. Rasch's view was that some of the condition, at any rate, was lupus erythematosus. The patient was suffering from inoperable carcinoma of the rectum. With regard to Dr. MacLeod's remarks, in none of Civatte's cases was there any eruption on the trunk. Civatte discussed cases of poikiloderma atrophicans vascularis, and gave good reasons for separating this condition from the one under discussion. In answer to Dr. Whitfield, he (the speaker) had noted that the patient complained very much of flatulence, but it was difficult to believe the eruption could be rosacea, partly because the pigmentation was so intense, and partly because there was definite atrophy, which Civatte had confirmed by histological examination.

Sarcoid.

By H. W. BARBER, M.B.

MISS H. H., aged 56, was referred to me by Dr. A. F. Denning on February 19 of this year for a chronic eruption of the face (sarcoid), and an acute outbreak of erythema multiforme on the hands, arms, and thighs.

Her family history is remarkable and must be emphasized. She was left an orphan at nine years of age; both her parents, a paternal aunt, her two brothers and her sister all died of tuberculosis.

Her own general health has been fair on the whole, and she is not aware of having had any tuberculous infection; but she has had two operations on her nose and has recently been troubled with bronchitis and lumbar pain.

The eruption on the face has been present for about five years. It consists of a large patch of nodular infiltration occupying the greater part of the right cheek; a nodule on the left side of the nose, and another smaller one on the left cheek. The appearances are characteristic of Boeck's sarcoid.

Patient was admitted to the private ward of Guy's Hospital for the following investigations :—

Wassermann Reaction.—Negative.

Von Pirquet Reactions to both human and bovine tuberculin completely negative (Dr. Eyre).

Sputum.—No tubercle bacilli were found.

¹ C. RASCH, "Poikiloderma Atrophicans Vasculare," *Brit. Journ. Derm.*, 1925, xxxvii, p. 477.

X-ray Examination (Dr. Lindsay Locke).—*Chest*: "Heart-shadow rather large to the left side. Diaphragm moves evenly and well. Costo-phrenic angles clear. Infiltration in both lungs made up chiefly of coarse striation with some old dense foci at right apex, ? old phthisis." *Hands and Feet*: "Right hand shows small translucent area at the head of the first metacarpal and tip of the terminal phalanx of the fifth digit."

Tonsils: Not obviously septic or infiltrated. *Teeth* (Mr. Kelsey Fry): An abscessed tooth in the lower jaw. It was not thought justifiable to make a biopsy.

Progress and Treatment.—While in hospital injections of sodium morrhuate were begun—three per week—as suggested by Dr. A. M. H. Gray, and these have been continued by Dr. Denning since her discharge. She was also given iodine and cod-liver oil internally. Unfortunately extraction of the abscessed tooth was followed by necrosis of a piece of bone and considerable inflammation; when this was at its height another slight outbreak of *erythema multiforme* occurred. She has now had nineteen injections of sodium morrhuate in all. There is very evident improvement with respect to the lesions, the nodules having become flatter and smaller.

Discussion.—Dr. J. H. SEQUEIRA (President) asked whether Dr. Barber would have expected to find active phthisis in this case.

Dr. BARBER (in reply) said that in all Schaumann's cases, when phthisis developed the skin lesions disappeared.

Multiple Occupational Squamous Carcinoma in a Gunsmith.

By W. J. O'DONOVAN, M.D.

THIS case is of some sociological importance, as I think it is the first case of the kind shown at this Society. The typical multiple squamous-celled carcinomata are, I think, not due to pitch or tar, but to oil. The man is 55 years of age; he has been a gunsmith thirty-nine years, and during most of that time his clothes have been saturated with oil. During and since the war he has been working under the same greasy conditions. Among the oils he handles are paraffin, Rangoon oil, and vaseline. He has had fifteen of these tumours cut out, and the gravest operation was the removal of nearly all his nose. Four of these tumours have been submitted to microscopic examination, and they have been squamous carcinomata. So far, he has had no adenopathy. He has asked us to certify that his condition is due to his work, but such a certificate is new to me, and we thought we would first submit the case to our colleagues.

Tumours are present on the scrotum, limbs and ears. There is no pigmentary change. The backs of the ears are studded with comedones.

Dr. J. H. SEQUEIRA (President) said that the man's financial future very much depended on the certificate which would be given. It was known that the repeated impact of oil on the scrotum in mule-spinner's cancer could produce squamous carcinoma; but the present case was an unusual one because of the exceptional occupation of the patient. He understood that the Home Office was not acquainted with any such condition.

Acne Agminata.

By G. B. DOWLING, M.D.

PATIENT, a young woman, aged 24, has an eruption consisting of reddish-brown papules embedded in the skin, arranged, for the most part, in groups upon the nose and infra-orbital regions, with a few isolated papules upon other parts of the face. On diascopic pressure they present the appearance of isolated lupoid nodules. The von Pirquet test is positive; this is a point of some interest, since the view has been expressed that acne agminata may be identical with Boeck's sarcoid. If

Schaumann's statement that the von Pirquet test is invariably negative in Boeck's sarcoid is accepted, this fact would prove that the two conditions are not identical. She has been treated with intramuscular injections of sodium morrhuate and with angiolympe, but neither drug has produced the least effect. She is now undergoing a course of carbon arc light baths, and her condition is showing some improvement.

Discussion.—Dr. H. C. SEMON said that he showed a somewhat similar case in a middle-aged woman two months ago, to whom morrhuate of sodium and carbon arc light were given, and there was preliminary improvement. This, however, had not been maintained, and she was still, while under treatment, developing fresh lesions. In the case referred to there was a typical epithelioid structure in an excised nodule, suggesting a tuberculous aetiology. There was serious general enteroptosis, and he wondered whether the skin condition was related to gastric and intestinal disturbance, as seemed likely. Though the von Pirquet reaction in the case was moderately strong, it was not very definite, and he thought intestinal toxæmia might be an adjuvant factor in the causation of the lesions in this case.

Dr. W. J. OLIVER said that he hesitated to accept the diagnosis of acne agminata in this case; it was not acneiform or pustular like the other cases of that condition which had been shown before the Section. As the von Pirquet test was so strongly positive, he would consider the diagnosis of disseminated lupus to be the more probable one.

Dr. H. C. SEMON (in reply to Dr. Oliver) said that in his own case there was no tendency to pustulation, nor even to necrosis; it was lupoid in type, as in Dr. Dowling's case.

Dr. H. W. BARBER said he thought that acne agminata was the condition which the French called miliaire lupoid, and he did not think there was ever necrosis of the lesions; those of acnitis, however, were necrotic. If these lesions were pressed with a glass they looked like the nodules of ordinary lupus.

Dr. H. G. ADAMSON said that he would regard this case as an example of Crocker's acne agminata. Although the microscopical appearances were closely similar to those of a papular-necrotic tuberculide, he did not think that acne agminata was so clearly of tuberculous origin as the papular-necrotic tuberculide. Acne agminata occurred mainly on the face, and the lesions, although they might show pustular heads, did not necrose to the same extent as did the lesions of the papulo-necrotic tuberculide, the distribution of which was also usually over the limbs. He said he would regard acne agminata as identical with acnitis and the papulo-necrotic tuberculide the same as folliclis or acne scrofulosorum. Neither of these eruptions was miliaire lupus, which was a true lupus.

Dr. DOWLING (in reply) said that acne agminata was never pustular. With regard to Dr. Semon's case he (the speaker) wondered whether the lesions in cases of lupus would disappear under treatment by general light baths, without the addition of local treatment. Complete regression of the lesions in cases of acne agminata could not be expected from treatment by general light alone, but might be effected if Finsen light was used also.

Premycosis.

By WILFRID FOX, M.D.

FOR the last twelve years this woman, aged 47, has been developing these diffuse patches. There are various points against the diagnosis of a premycotic eruption. There has been no itching and until now no ulceration. There are some signs of regression, but the patches always come back in the same place. When I saw the case a month ago the eruption was scarlatiniform. Three-quarters of a pastille dose of X-rays was applied to all the patches, and it made some difference to them, but did not clear them up in the way one would expect in mycosis fungoides. In one patch the treatment produced a small necrosis, although the dose was very small. The other diagnosis which suggested itself to me was that of xantho-erythrodermia perstans of Crocker.

Dr. J. H. SEQUEIRA (President) said that the absence of itching in an eruption which had persisted twelve years was an important point against the diagnosis of mycosis fungoides, and he asked whether a biopsy had been done. [Dr. WILFRID FOX: No.]

? Lupus Erythematosus : Pernio Variety.

By WILFRID FOX, M.D.

PATIENT, a man, aged 26, who came back from India last April, where he had suffered much from malaria. In November this eruption came out on the nose and cheeks. The infiltrated area was then much bluer than now. It has never been tender nor has it caused him inconvenience. He says he feels the cold a good deal, but he has never suffered from chilblains, and there is no sign of tuberculosis.

Case of Acute Nodular Leprosy.

By E. G. GRAHAM LITTLE, M.D.

PATIENT, a Burmese barrister, who has been six months in this country, reading for the Bar. His doctor has been observing him for the last two or three weeks, and confirms the statement of the patient that the eruption appeared about May 4, that is, ten days before he saw me. It came out suddenly on the face—a heavy crop of nodules, which were not uncomfortable or itchy. But before any eruption was seen, he had had very severe pain in the left arm, from the axilla to the wrist, and the ulnar nerve remains swollen and tender. The eruption appeared three weeks after the first pain. He had had no drugs preceding the occurrence of the eruption, though local applications were used for the pain. When the eruption was noticed, the doctor thought it was urticaria, and gave him calcium lactate, and that is the only drug he has taken. The eruption spread on to the hands, and then a very remarkable patch of infiltration, approximately 4 in. by 2 in., was noted on the left forearm about 4 in. from the wrist—a large dusky, flushed area, with much induration. A similar large red patch of induration developed on the back. He had definite syphilis eight years ago, in Burmah. I suggest that the present rash is a lepride, of very acute onset, and I think that that diagnosis is unavoidable.

Discussion.—Dr. J. H. SEQUEIRA (President) said the Section was grateful to Dr. Little for showing this case, and to the patient for coming to the meeting. Cases of leprosy were sufficiently rare in this country to make it desirable that the Members of the Section should see every one, as far as possible. The plaque lesion in this case exactly resembled that in a Polish woman who was under his own care not long ago, but it was a long-standing case, and that plaque was of slow evolution. The only case of the disease that he had seen in which there was an acute outbreak was that of a woman who came from South Africa. She went through the privation of the siege of Kimberley. She also had nodules on the cornea.

Dr. W. J. OLIVER asked whether this patient had been given iodides before the second rash came out, as such a drug made the leprosy rash much worse; it seemed to stimulate it.

Dr. J. M. H. MACLEOD said this case was interesting owing to the rapid development of the widespread eruption of nodules. Such outbreaks were met with not only in the early stages of the disease, but later; they might occur at any time in the course of a nodular case, when an attack of leprotic fever might be followed by an almost exanthematous outbreak of nodules. In a case recently under his care, that of a boy, in whom the disease had been in a quiescent state for about two years, an attack of fever had occurred; this was followed by an outbreak of nodules, practically all over the body, within forty-eight hours.

With regard to the question of what was best to be done, in the housing of a case such as Dr. Little's, it was beset with difficulties, as at the present time the disease was not notifiable in this country, and consequently compulsory segregation could not be enforced, in spite of the fact that many of those who had to do with lepers knew it to be a transmissible disease. He knew of three instances in which leprosy had developed in this country in individuals who had never been out of it, and obviously segregation was the most important measure in the prevention of the disease. It seemed to him, therefore, that the best plan would be for the patient to return home to Burnah if arrangements could be made for his transit.

66 Little: *Lichen Planus*; *Sarcoid*; *Erythematoid Epitheliomata*

Dr. A. WHITFIELD mentioned a case which the late Dr. Pringle brought to him sixteen years ago, that of an engineer who had been in the United States, India, China and South Africa. One night he assured the speaker that he went to bed feeling well; then he had what he called a malarial attack in the night, and next morning he had acute swelling of the face. He was seen ten days after the onset of the acute febrile attack, which was the beginning of the condition, and he then already had a leonine countenance. He (Dr. Whitfield) scraped a swelling just above the eyebrow with a cover-glass, and the stained specimen showed masses of *Bacillus lepræ*.

Dr. H. G. ADAMSON said that these cases seemed analogous to those of post-exanthematous lupus, which occurred after measles or other fevers in children who suffered from tuberculous glands.

Dr. GRAHAM LITTLE (in reply) said the doctor reported that there was no rise of temperature. The only drug he (the patient) had received was calcium lactate, and that was after the eruption developed. This patient was at present living in lodgings, and the question arose as to whether he should be allowed to continue to do so. Ought the case to be notified? Should he be allowed or encouraged to continue his studies at the Bar? Leprosy was not a notifiable disease, but seven or eight years ago a meeting of dermatologists took place in order to decide what steps should be taken with regard to a case of leprosy under the care of Dr. Stowers. It was decided to support Dr. Stowers in the opinion that it was not a very communicable disease, but those present had not felt happy about that decision.

Annular Lichen Planus.

By E. G. GRAHAM LITTLE, M.D.

THIS patient is a solicitor, who for six years has had a ringed eruption on the upper part of both legs and on the lower part of the sacrum. He has just come from abroad, where he saw two dermatologists, who both diagnosed syphilis, and the suggestion disturbed him. He came to see me six weeks ago. The eruption is annular throughout, and it is the only kind from which he has suffered. In all the Wassermann tests the reactions have been negative.

(?) Sarcoid.

By E. G. GRAHAM LITTLE, M.D.

THIS patient has indurated plaques,—small areas the size of a shilling, which have been noticed for the last six months. They have occurred chiefly on the back of the trunk, without any sensations of pain or discomfort. They are steadily enlarging and are increasing in number. He had a rib removed on the right side by Mr. Herbert Allingham twenty-seven years ago. At the hospital in which this operation was carried out not much information can be given me, but it is stated that there were swellings on the right side of the back, they were painless, and were found to fluctuate. They were incised and pus came out. One swelling would not heal, and finally a rib was removed. At that date the diagnosis was supposed to be tuberculosis. I suggest it is sarcoid, coming on after many years, possibly having as a first source a tuberculous rib.

Two Cases of Benign Erythematoid Epitheliomata.

By E. G. GRAHAM LITTLE, M.D.

Case I.—There is an isolated lesion on the dorsal surface of the sacrum, now the size of a sixpenny-piece, of two years' duration. It has an erythematoid aspect, and has a very fine rolled edge.

Case II.—In this case the disease is of much older date, a large rodent of the same type, which Dr. Adamson saw eight years ago, before we began to recognize

these cases. The patient has had a flat rodent, 3 in. by 2 $\frac{3}{4}$ in., under the left clavicle. I have brought her so that I may show the excellent effect of freezing. She has had nothing but freezing treatment for four years. At that time Dr. Adamson gave her X-ray applications, but these had no effect upon the patch. An exposure to the freezing over that area for not more than ten seconds in each area has produced a very good result. The area has so perfectly healed that Dr. Adamson at first thought it was sclerodermia. There is smooth skin, with very slight atrophy, on the surface. She has seven or eight of these patches, and the six others are in very much the same condition as four years ago when I first saw the patient.

Dr. H. C. SEMON asked whether there was any objection to excising this type of ulcer. Last week he had a case in which there were two of these typical flat rodents, with an eczematous appearance. He had recommended excision as the best way of getting rid of them.

Case for Diagnosis: ? Lichenoid Salvarsan Exanthem.

By W. N. GOLDSCHMIDT, B.Ch.

PATIENT, a male, aged 52, who came to the V. D. department last April on account of chronic superficial glossitis. His Wassermann was positive, and he was given novarsenobillon and bismuth; he stood two injections of 0.9 gm. novarsenobillon quite well. After the third, however, he said he "felt queer" for three days. In three weeks he was given another dose, and then he developed a rash on the body, and was admitted to hospital. This rash rapidly became exfoliative in character, but it remained confined to fairly definite patches on the limbs and trunk, and did not become universal. It was treated with collosol sulphur, but with only slight improvement. A month later the patient was also suffering from boils, which were successfully treated with collosol manganese. The rash was very irritable but otherwise he did not feel ill, and he had no rise of temperature. At this stage three injections of sodium thiosulphate were given, and these caused a definite improvement. The blood-count showed definite eosinophilia and a diminution of lymphocytes. After a few weeks of treatment in the ward the irritation disappeared, but patches of scaly dermatitis remained, though they faded somewhat. At that period the rash looked like parapsoriasis en plaques. But the intense irritability and absence of mica-like scales are against that diagnosis. A month later there was a recrudescence; he came into the hospital again, and after a few weeks the irritation again disappeared, but the patches were still there. At this time several groups of hyperkeratotic follicular plugs were noticed. He still has a rash on the body, but in the interval this has gradually changed its character; the scalliness has almost disappeared, and the colour has changed to that of lilac. The arrangement is rather reticulate, and in the middle of these rings there is a commencing atrophy. The lilac parts surrounding the atrophy show, in certain places on the back, some papules which resemble lichen planus, but in the front that is not distinct, and they seem to consist of dilated vessels with some hyper-pigmentation. Here and there are clusters of lichen spinulosus. A short time ago the rash as a whole reminded me somewhat of poikiloderma atrophicans of Jacobi. Now it is getting more like lichen planus atrophicus. Such a diagnosis would be strengthened by the presence of numerous and increasing areas showing lichen spinulosus. The possible diagnoses appear to be (a) poikiloderma atrophicans, (b) salvarsan dermatitis resembling lichen planus (several examples of which have been recorded), or (c) lichen planus atrophicus, apparently determined by the injections. With regard to (b), I do not know whether salvarsan dermatitis ever leads to such patches of atrophy. As to (c), it must be emphasized that it is only during the last few weeks that the eruption has begun to resemble lichen planus. Until then such a diagnosis was never dreamt of.

Discussion.—Dr. H. G. ADAMSON said that the general aspect of this case suggested to him lichen planus. One point in favour of that was the presence of lichen spinulosus. He had never seen, in an adult, lichen spinulosus unassociated with lichen planus.

Dr. J. H. SEQUEIRA (President) said he thought this case came into the class of lichen plano-pilaris, which the late Dr. Pringle described. He had not seen a salvarsan dermatitis resemble the condition presented by this patient.

Dr. WILFRID FOX regarded it as lichen planus but thought it was probably due to salvarsan. He had had two cases of typical lichen planus which came out during salvarsan administration, and it was one of the rashes described in connexion with the Manchester arsenic epidemic.

Dermatitis Artefacta.

By J. M. H. MACLEOD, M.D.

THE patient, a young woman with a syphilitic history, presents peculiar elongated lesions on the legs. These lesions are irregular in outline, and are either covered with a blackish hæmorrhagic crust, or are smooth on the surface; they are indurated, and have a granulomatous appearance. The variation in the type of lesion, the curious dark crusts covering them, their shape, and the presence of certain excoriations over them, suggest that they are artefacts. It is possible that in the case of the indurated lesions the friction, or whatever means has been employed in causing them, has resulted in the production of an artefact on a syphilitic basis.

Discussion.—Dr. J. H. SEQUEIRA (President) said that from the shape and distribution of the eruption he was of opinion that it was an artefact dermatitis, and that the changes now seen were secondary. One plaque was warty from a secondary hyperkeratotic change. The dark coloration he thought was blood-pigment.

Dr. H. G. ADAMSON agreed that lesions of this peculiar pattern and distribution must be artefacts. The patient could produce such by wetting her finger and rubbing the skin up and down. If the rubbing was persisted in, an erosion occurred. This present patient had a septic mouth, and he thought the excoriations had become infected with the saliva. The lumpy lesion might be produced by constantly pinching the skin.

Section of Dermatology.

President—Dr. J. H. SEQUEIRA.

Angioma Serpiginosum.

By J. H. SEQUEIRA, M.D.

PATIENT, a lady, aged 34, who has a spreading vascular eruption on the lower part of both legs. It has been noticed on one side for fifteen years, and on the other side for ten years. It is characterized by closely-set leashes of vessels forming a network, with outlying minute red spots which have gradually spread into the healthy tissue. I take it to be a case of angioma serpiginosum, which Hutchinson described as "Infective Angioma." The elements exactly resemble a case which I published with coloured plates in 1912'. Whether it can be regarded as nævoid or as a slowly spreading infection is a matter for further consideration. The patient complains of generally bad circulation, and suffers from chilblains on the hands and feet. There is nothing of importance in the family history.

Pityriasis Rubra.

By A. WHITFIELD, M.D.

I AM not quite happy about the diagnosis of this case. Patient is a gardener, who came to us ten weeks ago. He has had his present eruption for between one and two years, and he says it began on the inner sides of the thighs. When I first saw him I made a provisional diagnosis of primary pityriasis rubra, of the Hebra type. He was very red. He is under 50 years of age, and he has a hide-bound condition of his skin all over his body. His nails are not affected, except that there is a hyperkeratosis of the nail-bed; the nail-plate is not disturbed, though the nail is bowed over. I drew a pencil very lightly across the reddened area—so lightly that in factitious urticaria it would not cause a wheal, and in 15 to 30 seconds a large white stripe appeared in the pencil track. It is not a wheal, because passing the finger over it shows there is no increased density nor raising of the skin, but there is a faint sinking of the skin, due, I think, to the fact that the hyperæmia has disappeared. My belief, which can only be substantiated by a large number of cases, is that when the condition is well marked the diagnosis of primary pityriasis rubra is practically clear. It has been present in all my cases of pityriasis rubra, but not to any marked extent in any other case. We took him into hospital and investigated his condition as much as possible, and we carried out a blood-count. It is not the blood-count commonly found in pityriasis rubra; there is usually a certain amount of polynuclear leucocytosis with a slight rise in the eosinophils, up to 3 per cent. or 4 per cent. This man has 18,000 leucocytes. He has 44 per cent. eosinophils, a percentage with which I am not familiar in any skin disease except in the pemphigus group. There is nothing abnormal in the urine. We had cultivations made from his feces, and when he came in there was a considerable number of non-lactose fermenters. These we have eliminated, but he is not much better. Seeing that there were so many eosinophils present I thought it wise to give a colossal dose of thymol, in order to see if we could find parasites in the intestine, but we found neither worms nor eggs. Finally, we had a piece taken out, and that shows appearances which I have not hitherto seen in pityriasis rubra lesions. There is a belt of lymphoid infiltration just below the bases of the papillæ, and the epithelium is

¹ "Angioma Serpiginosum," J. H. Sequeira, *Brit. Journ. Derm.*, 1912, p. 355.

fairly normal. There is a very great increase in the waviness of the epidermo-papillary line, the result of his chronic inflammatory trouble. Among the masses of lymphocytes at the bases of the papillæ there are, in several places, many large irregular multinuclear cells. In a case published many years ago there were said to be tubercle bacilli. We have not found organisms in this case. The man is better, because he has been in bed ten weeks. I cannot say that any remedy I have applied has done him good. He is troubled with a considerable amount of itching. He has received doses of thyroid and small doses of opium in order to quieten down the skin.

Discussion.—Dr. H. G. ADAMSON said an interesting question in connexion with pityriasis rubra was whether it was due, in any particular case, to an internal toxin or to an external irritant. There was no sharp line to be drawn between the recurrent scarlatiniform erythema and pityriasis rubra. Recurrent scarlatiniform erythema might be due to drugs such as quinine or belladonna taken internally, but it might also be the result of either of these drugs applied to the skin. Pityriasis rubra might be set up by application of tar or mercury to the skin, and it might be brought on by arsenic injections. He now had in hospital a patient much like that of Dr. Whitfield's, also a gardener. He had been in the hospital twelve months. His eruption began when he was peeling off ivy from a wall, as a dermatitis of the legs, and there had gradually developed a generalized pityriasis rubra. During the twelve months he had continuous universal redness and desquamation with repeated exacerbations, and only now was he recovering. Lately the man had developed neuritis, with numbness of the hands and feet, and although the long illness had apparently been started by an external irritant, the occurrence of neuritis seemed to suggest that it might have been really due to some internal toxæmia.

Dr. WHITFIELD (in reply) said he agreed with what Dr. Adamson had said, except that he did not think that the presence of neuritis was necessarily in favour of an internal toxæmia being the cause. He had seen severe neuritis of the arm associated with epidermophytosis of the feet, and he thought the neuritis was produced by the septic absorption from the skin disease.

Case of Acrocyanosis.

By F. PARKES WEBER, M.D.

THE patient (M. P.) is a well-developed English girl of Hebrew parentage, aged 18. She has always tended to redness or lividity in the upper and lower extremities, even in warm weather, though by holding up her hands and warming them she could at times make them look much more normal. She has likewise always been subject to bad chilblains on the hands, and was so formerly on the feet also. As a result of last season's chilblains the finger-nails are much deformed.

Roentgen skiagrams of the hands show nothing abnormal. The Wassermann reaction is negative. Menstruation began at 14 years of age, and since then has been fairly regular. On the father's side of the family there is said to be a tendency to abnormal redness of the hands. The patient's blood-pressure is 140 mm. Hg (systolic) and 80 mm. Hg (diastolic). There is nothing abnormal in regard to her tonsils and mouth; her teeth are in good condition. The thyroid gland is not enlarged. She does not suffer from constipation. There is no evidence of tuberculosis anywhere, or of any disease of the thoracic or abdominal viscera.

The absence of cyanosis in the face and ears confirms the view that in cases of the kind the peripheral circulation in the capillaries of the upper and lower extremities—rather than the heart—is at fault. It is probably wrong to regard "chilblainy" acrocyanosis of this type as a variety of Raynaud's disease. The condition seems to be due to a chronic, more or less constant, *atonic* dilatation of the blood-capillaries and the other minute blood-vessels of the extremities. There are no paroxysms, as in true Raynaud's disease (Raynaud's syndrome), in which there are paroxysms of local cyanosis ("local asphyxia") or angiospastic pallor ("local syncope"), which may be succeeded by hyperæmic redness.

Thyroid treatment has previously been tried without benefit. Hot air baths and alternating hot and cold baths for the hands are now being tried, as well as intravenous calcium therapy. But the hands are still cold and red, and the feet and legs up to the knees show blotchy redness and cyanosis. I should like to hear the experience of others in regard to prognosis in such cases.

ADDENDUM (September, 1926).—Since the meeting I have had another quite similar case of acrocyanosis in a young woman, aged 23. In the latter case, however, it was associated with mitral stenosis, and, though it was obviously not caused by the heart disease, it was intensified thereby.—F. P. W.

Discussion.—Dr. A. WHITFIELD said he knew of a family who had this condition, and the members often became affected with subcutaneous hypertrophy. After a time the fingers became fat, and still remained somewhat blue. He recommended Dr. Weber to try soaking this girl's extremities in a very hypertonic salt solution, to the degree of putting 5 lb. of salt into every ten gallons of water. The immediate result of that he had found to be remarkably good; it quickened the circulation in the parts and restored the tone, the effect lasting for quite a long time. Grease might also have to be applied, as the treatment made the skin very dry.

Dr. S. E. DORE said he had brought for inspection a case for comparison with that shown by Dr. Weber. The patient, a girl, aged 21, had been affected with a very similar condition, both summer and winter, in the hands and feet and the lower third of the legs. The affection in the latter was a good example of the condition to which the term "artificial stocking dermatitis" had been applied. Another case had been under his care in which the patient had been similarly affected for thirteen years, in all seasons; her state was worse in the winter, when there were bullæ on the ankles. He (Dr. Dore) had tried vaso-dilators and vaso-constrictors, also endocrines, but he had been unable to influence the eruption. Dr. Douglas Heath had made an important observation when looking at this case, namely, that the patient had had tonsillitis, and he had remarked that in many of these cases the tonsils were septic.

Dr. AGNES SAVILL said that she had had a number of cases of this kind, and in all of them some toxæmic condition had been present. Often these girls had a loaded cæcum; in others the tonsils were in a bad state, and others had defective teeth. Some had developed the condition between 30 and 40 years of age, but the majority of cases occurred in young girls, who seemed normal, except for getting tired too readily. The appropriate treatment appeared to vary with each individual. She (Dr. Savill) had published one remarkable case in which the patient recovered because the treatment, namely, sinusoidal baths to the legs, was persevered with for many months. For nearly nine months the patient had a weak dose, practically every day, and was at the same time treated with an autogenous *Staphylococcus aureus* vaccine obtained from the urine. She had been suffering for years, but within a year of beginning the treatment she had normal thin ankles, feet and legs, as well as hands. Another case responded immediately to parathyroid medication. The majority of such cases were associated with pituitary deficiency, with characteristic abdominal and costal pads, and deficient menstruation. They responded to pituitary extract given by the mouth, provided all sources of toxæmia were dealt with at the same time.

Dr. SEQUEIRA (President) said that he had spoken to Dr. Woods, who was in charge of the Electrical Department at the London Hospital, and he agreed that there was a condition, usually regarded as a chilblain type, which was generally benefited by electrical baths. But there was another group of cases which was very likely due to focal sepsis. There was also a third class, which French dermatologists particularly believed to be associated with tuberculosis. He (the President) found that they derived definite benefit from very small doses of tuberculin. He considered the condition a symptom-complex, and thought that Dr. Weber rightly questioned whether such cases should be assigned to the category of Raynaud's disease, which was a paroxysmal condition.

Dr. PARKES WEBER (in reply) said that an occasional connexion between acrocyanosis and tuberculosis was fairly generally acknowledged. He thought that the sluggish condition

of the bowels in some cases of acrocyanosis might be explained as due to a general atonic condition of the unstriated muscular structures, with which the blood-capillaries were at least allied. He hoped that a trial of concentrated saline baths, as suggested by Dr. Whitfield, might be carried out at Droitwich.

Recurrent Bullous Eruption on the Feet in a Child.

By F. PARKES WEBER, M.D.

THE patient is a well developed boy, aged 4, who, since the age of one year, has been subject to the formation of numerous large bullæ on his feet—especially on the soles of the feet—in warm weather. Recently some of the bullæ have had sero-sanguineous contents. He has never had bullæ elsewhere, except one rather small one (quite recently) on the perineum. I can find nothing else abnormal about the boy. Wassermann reaction: negative. He is the only child of apparently healthy parents, and there is no history of any similar complaint in relatives.

I suggest that the case is a mild atypical form of epidermolysis bullosa, the exciting factor being irritation of the feet in moist socks during warm weather. The points against this suggested diagnosis are:—(1) the absence of ordinary traumatism as a direct exciting agent. I failed artificially to produce a bulla by moderate rubbing of the dorsum of either foot; (2) the hands, nails and face have not yet been affected; (3) the absence of any familial history of the disease.

If my suggestion be correct the treatment should consist in keeping the skin of the feet dry and suitably "ventilated." I have not noted any obvious hyperidrosis (dysidrosis) of the feet or other parts of the body.

ADDENDUM (September, 1926).—Under local treatment in the hospital by a weak formalin solution and an astringent lotion the bullous eruption rapidly disappeared (there were only traces remaining at the date of the meeting), but when the treatment was discontinued the bullæ reappeared. I have heard from the child's parents that some of them are hæmorrhagic. Since the meeting also there was for a time troublesome facial impetigo.—F. P. W.

Dr. J. H. SEQUEIRA (President) said he did not recall a case in which traumatism was not a factor, the traumatism being very slight, such as would not damage normal skin. And he had not seen epidermolysis bullosa limited to the feet; the lesions were always more general.

Erythema Elevatum Diutinum (Crocker).

By W. N. GOLDSCHMIDT, B.Ch.

PATIENT, a baby girl, aged 4 months. A month after birth mother noticed a lump on the right buttock, which at first was white and then gradually grew larger and became purplish red. During the last month there has been no visible change. The lesion is 1 in. long, $\frac{3}{4}$ in. broad, smooth on the surface, very deep red, with a regular, sharply-defined border, and raised about $\frac{1}{8}$ in. above the surrounding skin, which is perfectly normal. It is of firm consistency, and on picking it up the edges are easily felt, as if a piece of stiff leather was embedded in the skin. In the neighbourhood of this main lump are three or four nodules about the size of small peas felt deeply embedded in the skin, which is slightly discoloured.

Clinically, I thought the condition corresponded almost exactly to the cases of erythema elevatum diutinum described by Crocker, Williams and Judson Bury. As this is now generally considered to be a variant of granuloma annulare, I looked through Dr. Little's review in the *British Journal of Dermatology* for 1908, but I could not find a case which corresponded histologically with mine, except perhaps

one of Quinquaud's cases which was described as "fibrome fascicule." Stillians reviews the subject in the *Journal of Cutaneous Diseases*, September, 1919, p. 580, but I have not had an opportunity of consulting this paper.

I excised one of the outlying nodules, which the mother considered to be about six weeks old. The histology shows a very extensive, but irregular and diffuse, infiltration, consisting almost entirely of fibroblasts and, in places, of young fibrous tissue. No other kinds of cells seem to be present in excess, except perhaps a few lymphocytes. It apparently starts around the deep vessels of the corium and penetrates deeply into the fat and upwards into the middle of the cutis. There is relatively little new formation of blood-vessels. The original blood-vessels are not thrombosed, as they often are in granuloma annulare, and there is no area of necrosis.

There is no family history of rheumatism or of tuberculosis, and the child herself appears to be very healthy.

The President (Dr. Sequeira) and Dr. Graham Little suggest it might be a keloid. Would this explain the outlying nodules? There is no history of trauma or other preceding lesion.

Dr. GRAHAM LITTLE said he did not think the histology supported the idea of it being erythema elevatum diutinum; he regarded it as keloid.

Folliculitis Decalvans, with Lichen Spinulosus.

By E. G. GRAHAM LITTLE, M.D.

THE patient, a woman, aged 35, with this complex was shown. A full report of the case will be contributed later.

Discussion.—Dr. G. B. DOWLING said that in 1924 he had shown before the Section a case of cicatricial alopecia following lichen plano-pilaris. The case had been exhibited previously for the lichen plano-pilaris alone, the patches of alopecia developing at the time when the general eruption had practically cleared up. As far as he knew the cicatricial patches on the scalp had not there been preceded by lichen spinulosus, and would seem to correspond therefore to the second class of case of which Dr. Graham Little had just spoken, namely, lichen planus accompanied by patches of smooth atrophy of the scalp.

Dr. J. H. SEQUEIRA (President) said that there was a congenital anomaly which closely resembled this condition, namely, follicular ichthyosis of congenital origin associated with baldness. Dr. MacLeod had reported three cases,¹ with a review of the literature.

Erythematoid Benign Epithelioma.

By E. G. GRAHAM LITTLE, M.D.

PATIENT a lady, aged about 74. She has suffered from psoriasis for many years, and has patches upon the elbow and back of the trunk. The epithelioma now seen did not apparently develop upon a psoriasis patch, but upon the healthy skin covering the left breast. Its onset appears to have occurred at some time preceding 1914, and the growth seems to have approached the nipple; apparently because of its neighbourhood it was regarded as Paget's disease, and, in 1922, the left breast, including the nipple, was removed at the London Hospital. The superficial epithelioma has slowly spread, and now covers an area of about 6 in. by 6 in., showing the characteristic erythematoid aspect, with numerous pustules upon the surface, and a somewhat ill-defined and definitely rolled edge in parts of the margin. The shape of the patch is very irregular, with serpiginous outline. There is no free ulceration anywhere, and no glands in connexion with it can be felt. The patient's general health is fair for her age. There are no other similar lesions elsewhere.

¹ J. M. H. MacLeod, *Brit. Journ. Derm.*, 1909, xxi, p. 165.

Dr. J. H. SEQUEIRA (President) said he did not remember the case, but apparently four years ago he had made a diagnosis of Paget's disease and recommended amputation of the breast, which was carried out by Mr. Openshaw. The operation was done privately and unfortunately no histological examination of the tumour was made.

Numerous Sarcoids of the Erythema Induratum Type.

By E. G. GRAHAM LITTLE, M.D.

PATIENT, a young girl, aged 18, with a previous history of tuberculous glands in the neck. The lesions occupy the leg and lower part of the thigh; one of those in the lower leg has begun to break down and suppurate, leaving a deep sinus.

Glossitis Migrans.

By E. G. GRAHAM LITTLE, M.D.

THIS patient has been shown recently by me, and is now again brought forward because the organism isolated from the lesions upon the tongue has been cultivated anaerobically on glucose agar. A pure culture of a large Gram-positive coccus, not unlike any streptococcus and not arranged in chains, has been obtained. The patches upon the tongue have diminished, but have not disappeared under treatment by mouth-washes of peroxide of hydrogen.

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PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED BY
SIR WILLIAM HALE-WHITE, K.B.E., M.D.
AND
T. WATTS EDEN, M.D.

UNDER THE DIRECTION OF
THE EDITORIAL COMMITTEE

VOLUME THE NINETEENTH
SESSION 1925-26

SECTION OF ELECTRO-THERAPEUTICS



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SECTION OF ELECTRO-THERAPEUTICS.

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The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Section of Electro-Therapeutics.

President—Dr. STANLEY MELVILLE.

The Organization and Work of a Light Department in a Surgical Tuberculosis Hospital.

By Sir HENRY GAUVAIN, M.D.

By light treatment is meant treatment by light produced by artificial means in distinction from sunlight. Only since the end of the war have I been able to realize a cherished ambition to have a properly equipped light department at Alton. I have long been convinced of the value of sun treatment of surgical tuberculosis, and on the ground of that practical experience rather than on the scientific principles of light therapy (which are not yet fully established) have I found justification for a department in which artificial light sources are employed to supplement or take the place of sunlight.

Light treatment is necessarily very expensive. The initial cost of the lamps is only the beginning of a considerable and constantly recurring expenditure. At Alton an admirable generating plant in charge of a highly-skilled engineer is available, so that it is a comparatively simple matter to select a ward as near to the power-house as possible in order to reduce the length of cable, and to dig a connecting trench in which two cables are laid. By the kindness of Dr. Axel Reyn, whose paper read at the British Medical Association Portsmouth Meeting, in 1923,¹ has proved very useful in this connexion, I have been permitted to study the methods employed at the Finsen Institute at Copenhagen.

Dr. Reyn and his co-workers pin their faith to the open carbon arc, both for the general light bath and for local treatment. At Alton, however, I have decided not to limit the choice so rigidly; nevertheless, I make this source the principal one, and, determining that my own department should be based on the exact technique of the Finsen Institute in this respect, I succeeded in getting the services for six months of one of Dr. Reyn's trained sisters in order that the nurses in my light department might be instructed in the Finsen method.

The installation consists of two 75-ampère carbon arc lamps, each capable of treating simultaneously eight ambulant patients and three recumbent patients.

With regard to the other sources employed during recent years a good deal of attention has been given to short-wave or ultra-violet radiation, and the value of such radiation (in rickets particularly) has been demonstrated. Therefore, I make provision for mercury vapour lamp treatment in my department as well as for treatment by the tungsten arc, the iron arc, and other methods. The short-wave rays have proved somewhat disappointing. They have little penetrating power, although great superficial necrotic action, and I think it is very necessary to exercise caution in using them. Until more is known about their mode of action my whole instinct is to proceed very carefully indeed.

In the entire work of the department constant and responsible supervision is very necessary, and for this reason the department is so arranged that everything is under the immediate observation of the sister in charge. Treatment goes on ordinarily from eight in the morning until seven in the evening, after which every lens and

2 Levick: *Apparatus for the Production of Artificial Sunlight*

compressor is cleaned and the installation got in order for the next day. For general light baths a treatment lasting two and a half hours, and given on alternate days, is sufficient. While this treatment is being given the heads of the patients are protected by adjustable asbestos shields; the patients are given water to drink and at the conclusion the ambulant cases go away for a douche and the recumbent cases are thoroughly washed. By the use of compressors, which exsanguinate the part, much deeper penetration of the light becomes possible. I find it of great value to intermit the light baths after a certain period of treatment.

In the treatment of surgical tuberculosis I regard the Finsen method as the principal and the other light methods as accessory. The mercury-vapour lamp and the tungsten arc are not so valuable in the general treatment of this condition as are the carbon arcs, though they may prove useful to prepare the way for the latter, and they are certainly advantageous for local uses, as in the treatment of sinuses and discharging glands. The long-wave infra-red rays are also of some value in local treatment, though I am doubtful about the claims sometimes made on their behalf. I have also a 110-volt Kromayer lamp, which I employ for local treatment.

The photographs I am exhibiting illustrate my apparatus, including a tunnel arrangement for subjecting a limb or the whole body to concentrated light. I am now experimenting on the production of portable lamps designed for the patients who are too ill to be brought into the department.

At Alton the light department has the great advantage of the exclusive services of a laboratory research worker.

[April 17, 1925.]

The Selection of Apparatus for the Production of Artificial Sunlight.

By G. MURRAY LEVICK, L.R.C.P.Lond., M.R.C.S.Eng.

I THINK that a paper discussing the choice of apparatus available for the production of artificial sunlight will be useful at the present time. It is a difficult subject, however, and the time has not yet arrived for laying down hard and fast rules, owing to the brevity of our experience, the diversity of opinion held by those of us who are studying this matter, and the difficult conditions under which it may be necessary to administer the treatment.

From the point of view of this paper, artificial sunlight must be understood to mean the general application to the body of those rays that are found in real sunlight, but not necessarily in the proportions in which they occur in nature.

The question chiefly troubling the minds of those doctors who are beginning to study the application of this treatment is, whether they should instal open arc lamps or mercury vapour lamps. I am convinced that any disfavour that may have overtaken the mercury lamp is chiefly owing to the erroneous idea that it is the ultra-violet rays alone that produce the therapeutic effects of sunlight, so that the mercury vapour lamp has been used alone and its effects compared with those of the open arc lamps. The energy brought by the electricity to the mercury vapour lamp is concentrated almost entirely upon the production of the ultra-violet and violet rays, the longer rays being present in a negligible proportion. I have found that by using the mercury vapour lamp in combination with the long ray lamps, which I designed for the purpose and will describe later, I have obtained much better results, therapeutically, over a large range of cases, than I have been able to obtain with the use of the open arc lamps.

At St. Thomas's Hospital I have been working with three complete installations of mercury vapour and long ray lamps, and have treated a variety of cases with

these. Simultaneously, I used an open arc lamp with carbons impregnated with nickel, and employed it in a separate room for a separate group of patients, varying in age from early childhood up to late adult life. These patients included cases of general debility without apparent cause, neurasthenia and chronic rheumatism, in fact, cases in which we have been accustomed to observe marked improvement or complete recovery under treatment with the mercury vapour combination. By comparison with patients of a similar type under the mercury vapour combination treatment, the effect of the open arc lamp was distinctly disappointing. I do not mean to say that the results were all negative, because some responded well, but many showed only moderate response, whilst some cases made no advance at all. These were adults suffering from debility and fibrositis accompanied by rheumatic pains. They had been under treatment for over a month, and they were taken off treatment from the open arc lamp and submitted to the mercury vapour combination with immediate benefit in every case. Shortly after this, so marked was the difference between the therapeutic effect of this open arc and the mercury vapour combination that we unanimously decided to close down the open arc apparatus.

At the Victoria Hospital for Children I used an open arc lamp with carbon terminals bored and packed with tungstic oxide. I came to the conclusion that the results obtained in treating debilitated, rickety, and tuberculous children were inferior to those obtained with the mercury vapour combination, and I therefore discontinued its use. In this case my observations were not so thorough as they were at St. Thomas's Hospital, and I may have been mistaken in my conclusion, but I do not think so.

At my clinic at Tufton Street, which was installed by the British Humane Association, we have a long flame open arc lamp and two complete mercury vapour combinations. If you go into the clinic when the latter are burning alone, the atmosphere is cool and exhilarating, with that peculiar freshness which the mercury lamp produces. Turn on the open arc lamp and in two minutes the place smells and feels like a laundry. The staff all say that they become enervated and listless when the open arc is in use. It burns up the oxygen, heats up the air and makes the atmosphere of the whole room stuffy; at the same time we cannot create a draught, as this causes the lamp to flicker.

This effect upon the atmosphere should be taken into consideration when planning the installation of artificial light for a clinic in enclosed quarters, because unfortunately the available quarters are not always ideal.

Another point in favour of the mercury vapour combination is its constant intensity. This permits a very accurate regulation of the dosage. Again, if it is desired to arrange any particular proportion of ultra-violet and the longer rays, this can be done with the greatest ease when a mercury vapour lamp is used, but such arrangement is exceedingly difficult when an open arc is employed.

Owing to the extreme intensity of radiation obtainable from a mercury vapour lamp with a small amperage, patients can be treated in a short space of time,—a matter of importance if they are being dealt with singly.

The mercury vapour lamp combination is in the long run much cheaper to use than an open arc, first, on account of the greatly reduced consumption of electricity, and, secondly, because a quartz tube in constant use will remain effective for a year or more and can be rendered effective for a further year at a moderate outlay. This remark applies to tubes with a permanent vacuum. Other mercury vapour tubes which are now self-exhausting are at present on the market. We do not yet know how long these tubes will last, so it is difficult to compare their efficiency with that of the older types.

There are tubes made in this country, with candle-power varying from 1,000 to 3,000. I think myself that a 2,000 candle-power mercury vapour lamp is sufficiently powerful in the hands of any but very experienced operators.

The most glaring faults common to all mercury vapour lamps that I have seen on

4 Levick : *Apparatus for the Production of Artificial Sunlight*

the market consist in the inaccessibility of the reflector and the inaccuracy of the focus. I therefore had constructed a lamp which overcame both these faults and this will shortly be purchasable. Duralumin is a very suitable metal as a reflector for the ultra-violet rays, and it is most important that it should be kept thoroughly burnished by someone who understands how to do this, and does not scratch the metal, because any dullness or scratching greatly impairs the power of refraction of the reflector. This is why it is so important to have the reflector removable so that it can be properly cleaned. In my new design the reflector, besides being removable, can be focused in relation to the light tube. These rays which proceed from the reflector are really very important, because they are parallel, and strike the surface of the skin almost vertically, thus penetrating more deeply than most of the rays coming from the tube, which strike the surface of the skin obliquely.

With regard to the long ray lamps, I have had these manufactured by an English company. They consist of globes fitted with a carbon filament *in vacuo* backed by a reflector on which they can be focused at will, and having in front a red glass screen which can be used when only the red rays are desired. Or they can be fitted with clear glass if all the visible rays are desired. Ordinary soda glass stained with gold chloride cuts down the heat rays ; if these are desired in full intensity the screen can be removed altogether.

I have mentioned above some of the advantages of this mercury vapour lamp combination. The disadvantages of the mercury vapour lamp consist in its requiring skilful handling on account of this extreme intensity, and in its emission of very short-waved ultra-violet rays. In skilful hands these are not disadvantages, but they have to be taken seriously into consideration when the lamps are to be used by any but skilful operators. On the other hand, most of the carbon arc lamps are certainly much safer if the treatment is required at, say, an infant welfare clinic, where the staff are not very skilled and the supervision by a medical man is not very competent. In this case it may be better to instal open arc lamps. Another advantage attaching to carbon lamps is that a number of patients can be treated at one time. On the other hand, the exposure will be much longer, and this almost neutralizes the saving in time obtained by means of these lamps ; but as I said before, the lower intensity of the rays from most of them is a great safeguard for the patient, as it allows a greater latitude of exposure. When carbon arc lamps are used at a clinic such as I have mentioned above, it will be better, in my opinion, to have benches or couches arranged at a fixed distance from the arc so that the patients are always treated by rays of, roughly, the same intensity. This is so important because the intensity of the light varies as the square of distance, so that a few inches nearer or further from the arc make a great deal of difference to the length of the exposure.

Debilitated patients, or any patients who cannot sit up for a long period without fatigue, should be treated in a reclining position. They should not have to sit for a long time in one position, as this forced, prolonged posture is very tiring for people who are ill, and may detract from the effect of the treatment.

The observations recorded in the above short notes were made in conjunction with close laboratory observations by skilled workers and are not the result of unchecked impressions. A great deal more could be written on this subject, but I think I have said enough in laying down the chief points that occur to me, and that may be helpful to those medical men who are beginning to study the treatment. I think I may say, in summing up, that in really skilled hands, that is to say in the hands of a doctor who has devoted considerable study to, and has had really practical experience in administering, artificial light, the mercury vapour lamp combination offers greater opportunities than the more crude open arc lamps. But a beginner may do well to commence with this latter form of apparatus.

I have not made any mention of the accessory apparatus, such as douches, fans, &c., that can so well be used in connexion with the light treatment, as these do not come within the scope of the present subject.

Section of Electro-Therapeutics.

President—Dr. ALASTAIR MACGREGOR.

Then and Now :

PRESIDENT'S ADDRESS.

By ALASTAIR MACGREGOR, M.D.

OUR previous Presidents have from year to year delivered inaugural addresses concerning various aspects of electrology and radiology—historical, educational, technical, clinical, prophetic, &c.

I, this evening, in assuming the honourable position to which you have been good enough to call me, propose to consider for a few minutes a wider subject, viz., the vast changes that have taken place in the science and art of medicine since I entered Edinburgh University as a student, now forty-five years ago. Some of you may think that the consideration of such a subject appertains more to the Section of the History of Medicine than to the Section of Electro-Therapeutics, but we must remember that electrology and radiology nowadays touch medicine and surgery at every point. Though but a section of the integral whole our relations extend to practically every branch of the science of medicine, a fact which was well brought out by both of the last Mackenzie-Davidson lecturers.

The up-to-date electrologist and radiologist must not only possess a thorough knowledge of electricity, physics and chemistry, as well as of anatomy, physiology and pathology, but above all, if he wants to realize the potentialities for good of his special work, he must also possess a good clinical knowledge of medicine and surgery in all their branches.

I therefore think that a short review of some of the most important changes and discoveries which I have noted during the last forty-five years is not inappropriate on this occasion. And what discoveries and developments there have been during that period! The new surgery rendered possible by the work of Joseph Lister, who saved more lives than Napoleon destroyed, and the discovery of X-rays and its wonderful developments, would by themselves make it notable; but in addition there have been the birth of bacteriology, with its vaccines and sera, the triumphs over anthrax, typhoid, diphtheria, tetanus, and many other diseases; the birth of parasitology, which by its triumphs over malaria and yellow fever has cleared the world of several white men's graves; the discovery of high-frequency currents and, later, of diathermy with all its developments; the discovery of Hertzian waves, the establishment of the electrical theory of matter and the recognition of matter as one of the forms of energy; the discovery of radium, the investigations of Leduc on the migration of ions, the introduction of the electro-cardiograph, and, last of all, the appreciation of the value of sunlight and ultra-violet rays in various maladies.

All through there has been a steady improvement in methods of sanitation, in the treatment of tuberculosis, and in infant welfare. The death-rate has been lowered, and a leading authority has recently stated that every infant born into this world alive has a sporting chance of living five years longer than its grandfather.

This is but an imperfect sketch of the sum total of the general advance in every subject in the science and art of medicine since the beginning of my student days. The happy union of societies now amalgamated in some four-and-twenty Sections under one common roof in this magnificent building would have been an impossibility (for want of scientific personnel) in these early days. This consummation is very largely, if not entirely, due to the wisdom and pertinacity of our late genial and

[October 16, 1925.]

energetic secretary, Sir John MacAlister, who devoted time and health to this, which one may almost call the offspring of his brain. In fact, the Council realize, and are sure the Fellows will also—that the Society, as at present constituted, owes its creation to his organizing powers, that its growth and success are chiefly due to his zealous devotion to his duties, and that its welfare and reputation have been his life's work.

To revert to less happy days. The astounding conditions that existed on the surgical side in pre-Listerian days can hardly be visualized by the student of to-day. The condition of the surgical wards must have been dreadful—healing by first intention was uncommon, healing by what the Irishman called “no intention at all”—otherwise sloughing—was far too common. Septicæmia, pyæmia, erysipelas, tetanus and various forms of gangrene claimed far too many victims. Therefore surgeons hesitated to operate unless no other course seemed open to avert otherwise certain death. This deplorable state of affairs had gone on from time immemorial and was still existent when Lister began as a surgical dresser in University College Hospital, London. It is said that in one of his early cases the patient developed phagedænic gangrene, and this so impressed him that he determined to make the discovery of the cause, prevention, and best method of treatment of these surgical pests his life work. After this beginning in London he went up to Edinburgh to study Syme's methods, which consisted largely of frequent dressings and scrupulous cleanliness. Later on Lister carried out a great deal of experimental work on the early stages of inflammation and the coagulation of the blood, and he came to the conclusion that the surgical catastrophes were closely connected with the putrefaction of the blood and serum in the wounds and subsequent systemic infection. The cause and best method of prevention of this putrefaction were still mysteries. There were various theories prevalent as to the cause of this putrefaction of wounds—such as the air of the operating room being too hot or too cold, or there being any air at all (and it was difficult to operate in a vacuum), the presence of so-called miasms (nobody knew what miasms were, but most thought that they were gaseous), the overcrowding of patients, “hospitalism,” or the unhealthy condition of the patient, and so on. Lister had been taught by Syme to observe scrupulous cleanliness. Lister used still more scrupulous cleanliness, yet he did not get healing by first intention as often as he desired.

When Professor of Surgery in Glasgow in 1864, Lister's attention was accidentally drawn by Professor Anderson to the work of a young French chemist, Louis Pasteur, who showed that putrefaction was due to minute living particles. This theory Lister immediately decided to apply to the treatment of wounds. As these so-called “germs” were supposed to be floating in the air, like vultures hovering over their prey, the question was how to prevent their access to wounds, and if, before the case was seen by the surgeon, the “germs” had succeeded in getting into a wound, how to kill them before they had had time to establish a footing. As Pasteur's methods of filtration or heat sterilization could not be applied to the treatment of wounds Lister saw that he would have to find some suitable chemical antiseptic. Reading in a newspaper that carbolic acid had been successfully used for the disinfection of sewage in Carlisle he decided to try it.

In time he used a solution of carbolic acid for his hands, for the patient's skin, for the surgical instruments and for the surgical dressings—also a carbolic hand spray, which was used during every operation and at every subsequent dressing. This antiseptic treatment was scoffed at, both at home and abroad, except by a few faithful followers, but in course of time several surgeons from all countries, especially Germany, began to visit Lister's wards in order to study his methods.

Sir Watson Cheyne, in the first Lister Memorial Lecture delivered at the Royal College of Surgeons of England on May 14, 1925, and afterwards published under the title of “Lister and His Achievement,” which is a book well worth studying,

gives a graphic description of the usual scene upon these occasions. Directly the bandages had been cut the dresser started his hand spray—each layer of the dressing when removed was handed round to each distinguished foreigner to smell in order to show that there was no odour or putrefaction present. When Lister came down to the so-called "protective" placed over the wound he peeled it off with a pair of forceps exposing the wound either soundly healed or covered by a solid, firm blood-clot and without any sign of inflammation or suppuration in the wound.

"As a rule," writes Sir Watson Cheyne, "this was followed by a sort of gasp of surprise by the distinguished foreigners, and then a violent conversation would break out among them, accompanied by equally violent gesticulations, so that one became alarmed lest the peace of the nations was going to be endangered. The poor dresser who was almost, and indeed sometimes actually, faint from the pumping of the spray, was for the time being completely forgotten. But however exhausted he was and however much his wrist and arm ached, not one of his dressers would give in and let Lister down."

In time, instead of the hand spray a spray worked by the foot was employed; then a spray on a pedestal worked by a sort of pump-handle (this was irreverently called the "donkey engine")—still later on a steam spray was used.

Lister continually laboured to improve his dressings and to find some antiseptic which would act as well as carbolic acid without its irritating properties. He used to fasten pieces of gauze impregnated with various kinds and strengths of antiseptics, by means of collodion or strapping on his arms to see whether they caused any irritation. Any antiseptic which caused no irritation was next tried on a small unimportant wound. Thus he came to use solutions of perchloride and biniodide of mercury and double cyanide gauze and gradually restricted the use of carbolic acid.

The military application of antiseptics which Lister suggested in 1870 was not adopted until late in the Franco-Prussian war, at least apparently by the French, because we read that there were rather more than 13,000 amputation cases recorded by the French, and that of these over 10,000 proved fatal. If the Germans did not adopt his antiseptic method at that time they evidently did so very soon afterwards, because when Lister made a tour through Germany in 1875 he received a magnificent reception at every place which he visited. When I started work as a surgical dresser fifteen years after the antiseptic treatment had been first introduced, the battle between the Listerians and the Anti-Listerians had been won by the former, in Edinburgh at least, but not in some other parts of the country, where surgeons still looked with satisfaction at their cases of amputation oozing with what was called "laudable" pus. Gradually, however, the antiseptic treatment, unmodified or modified, was adopted universally, except by some "die-hards" who scoffed at the germ-theory (so called) as being a silly fad and more particularly a Scottish fad, although Caledonia, stern and wild, could not claim Lister as a son—he having been born in Essex.

In 1886 Von Bergmann introduced steam sterilization of dressings and instruments (aseptic surgery).

In 1887 the use of the carbolic steam spray was abolished, as it was believed that the germs floating in the air were little, if at all, pathogenic. Some of the sprays were afterwards used by doctors for the treatment of whooping-cough—others came to rest on the shelves of museums.

I may have spoken too long about Lister, but he is a splendid example of dogged British perseverance winning through in spite of disappointments, scorn and obloquy. He always believed that his methods would in time bring surgical salvation to the world, and "to believe is often to know, and knowledge confounds all scoffers." He has made modern surgery possible, and to him, I feel, belongs the undying honour of having paved the way for a fuller revelation of the secrets of Nature, a revelation that has broken down the artificial barriers that had previously divided the profession and shown us the interdependence of every branch of research.

His epoch-making discoveries were certainly but the practical application of the knowledge conveyed by the researches of Pasteur and others to whom the microscope proved an indispensable aid, and thus was added another child to the family of medicine—viz., bacteriology. The microscope, too, had passed in its infancy through the period of doubt and obloquy. One can hardly realize that Lionel Beale, for instance, some years before, should have requested a friend who came upon him "looking through the end of a brass tube" (i.e., a microscope) to maintain secrecy lest he should be accused of quackery; but so it was.

Forty years ago there was a glimmer of the part microscopy was to play in the discoveries of those intervening years in which we have occupied the stage.

The bacillus of anthrax had been established by Koch in 1876-1877 as the living cause of the disease—the first disease in which a living organism was proved to be the specific cause. As a result of further research by Koch, and more particularly of Greenfield (of Edinburgh), vaccination of cattle, and especially of sheep, against anthrax, was in 1883 introduced by Pasteur in France. Such immense numbers of animals were saved by this means that Huxley said that France had gained from it alone enough to pay the whole Prussian War indemnity. About the same time, as a result of prophylaxis, the death-rate in Bradford from wool-sorter's disease was reduced some 90 per cent.

But our work as students was practically limited to the staining of cells of coarse pathological specimens. Even this foreshadowed the possibilities offered in the differentiation of diseases, and soon bacteriology was to occupy an outstanding position. Malaria, typhoid, typhus, tetanus, yellow fever, syphilis, and other ills have yielded to the spell. Indeed, so great is the field that specialization in this domain has become a necessity as the life-history and reactions of the many organisms call for special research. Diphtheria, too, has yielded. In 1883 Klebs discovered the bacillus and in 1884 Löffler showed that it was the cause of the disease. Yet it was not until 1894 that Emil von Behring began to prepare the diphtheria antitoxin on a large scale. Its value as a specific remedy, especially if administered sufficiently early, was soon established, and how many thousands of lives have been saved thereby.

The great improvements in the technique of microscopy lead one to hope for the speedy discovery of the cause of the acute specific fevers, and ultimately that of malignant disease, or at any rate the contributory factors to malignant disease. We all earnestly hope that the recent researches of Dr. Gye and Mr. Barnard may lead to a clearer conception of the prevention and cause and cure of that dreadful scourge—cancer.

The history of the medical triumph over malaria and yellow fever reads almost like a novel. You know the details as to how Laveran (a Frenchman) in 1880 discovered an organism in the blood of malarial patients; this organism was also found by other observers (mostly foreigners) in succeeding years. They were of the opinion that this was the malarial parasite, but the seed of discovery remained on fallow ground until it occurred to Sir Patrick Manson in 1894 that, just as in the case of filariasis he had found some years previously in China that the disease organisms were conveyed from man to man by a mosquito, the same conditions might obtain in the case of malaria. At his suggestion Sir Ronald Ross went out to India in 1895, and by 1897 Ross was able to prove that the blood-sucking intermediary was an *Anopheles* which bred in swamps and collections of stagnant water.

Ross started an antimalarial crusade by draining swamps and pouring paraffin oil on to the surface of water which could not be perfectly drained. Dr. Sambon and Dr. Low, of the London School of Tropical Medicine, went to the Roman Campagna at the height of the malarial season in 1900, and by means of wire-gauze nets at night-time protected themselves from the disease which was raging all around them. They sent infected mosquitoes to London which were allowed to bite Manson's son and a laboratory assistant, and both of them contracted malaria. Thus was it

definitely proved that malaria was transmitted by the *Anopheles* and that bad, marshy air (malaria) was not the cause.

The interesting fact was also brought out that the female insect was the aggressor—the diminutive male insect leading a blameless life on a diet of fruit juice, whereas Madame *Anopheles* demands more stimulating fare.

As regards yellow fever, which is caused by the *Stegomyia*, de Lesseps, after losing 50,000 workmen from that disease and from malaria, had to give up the attempt to construct the Panama Canal. Many years afterwards the United States Government realizing that the services of a medical expert were necessary, requested Gorgas to take command. As a result of his endeavours—screening patients, draining swamps, spraying with paraffin oil—not only was the construction of the canal completed, but the Panama zone—previously a white man's grave—was made so healthy that in 1907 there was only one case of yellow fever in that district.

Since my student days there have been immense advances in physiology, and the perusal of any recent book on this subject shows what a very live structure the human body is.

In my student days our knowledge of the constitution of the blood was limited to red and white corpuscles and plasma—enough to satisfy our examiners; but to-day there is a formidable literature for anyone who desires to study the blood alone, even to its chemistry. The biochemist has appeared on the scene and bewilders us with the results of his research, so different from the somewhat crude ideas accounted sufficient in our early days.

Under the name "metabolism" what a field of investigation has been opened out! The value of the various secretions of the internal organs were reckoned in simple terms; physiology had dealt with the more obvious secretions and excretions, and of these gastric juice and acidity formed the chief subjects presented to us. On the liver was heaped the opprobrium of most of human ills, but the biochemist has changed all this and we now know, or hope we know, more of the subtle changes and interchanges between our old familiar friends, and have been further introduced to some that work in a way scarcely dreamed of. Thus the hormones came into prominence, the thyroid, suprarenal, pituitary and other glands offer to the pharmacologist a large field in which to experiment; indeed, as in many another sphere of medicine, fashion may have outrun discretion, and the caution of the genuine scientific worker may have been dethroned by the empiric.

As regards therapeutics I must be brief. Since my student days many drugs have been introduced—some valuable, some worthless. The first notable introduction I remember was that of cocaine, which was first used by Köller, of Vienna, as a local anæsthetic in eye surgery. There was soon such a great demand for it that the wily druggist quickly raised the price of this alkaloid to one guinea per grain—"as dear as cocaine" was quite a byword in those days. The additions to the list of new remedies are now bewildering in number. Would it not be better if we acquired a thorough knowledge of the action of the older and more trustworthy remedies rather than prescribe new drugs of which we know nothing except what we read in the speciously written pamphlets which accompany the samples sent to us by enterprising chemists?

Now to come to our own special subject. In my student days in Edinburgh electrology was in a state of suspended animation—X-rays had not been discovered. My first (and only) recollection of any electrical apparatus was the faradic battery which was used (perhaps too vigorously!) for Saturday night "drunks," cases of hysteria (now called functional cases) and cases of opium poisoning. It was also used for the treatment of muscles wasted by the prolonged application of splints in cases of fracture. How different from the modern treatment of fracture with early movement and massage—the anodal galvanism of Heald, the sinusoidal current of Barclay and others.

I have no recollection of seeing in those days any galvanic battery at the hospital, and I doubt whether any contemporary has more than a hazy recollection of such an apparatus or of its use in the schools. For the emancipation of electricity from the thralldom of quackery which had long enslaved it, and for the diffusion of the uses and capabilities of electricity as applied to medicine, we have to thank Dr. Lewis Jones. Patient in working, lucid in explanation, generous in his sharing with others the fruit of his toil, his memory deserves to be cherished among us.

With the development of electrology you are all acquainted; for example, the high-frequency currents of d'Arsonval followed by the diathermy current of Nagelschmidt, used in medicine and surgery. The latest development is, as you also know, the use of diathermy in gonococcal infection; this very successful treatment we owe to the painstaking observations of Cumberbatch and Robinson. I have watched this method of treatment from its very conception down to its present condition of proved efficiency, with the greatest interest and admiration.

The discovery of X-rays by Röntgen was made just thirty years ago. Consider how it has fundamentally altered our ideas and our practice in physics, chemistry, and almost every branch of medicine. Even those who have worked at radiology ever since Röntgen's epoch-making discovery must have been astonished at the present magnitude of this very amazing subject which was evidenced by the valuable results presented to us in the *Transactions* of the recent Congress held in London. In fact, the subject of radiology has grown so much that in our Section it threatens to act like a benevolent cuckoo and push electrology out of its nest. Concerning radium (introduced in 1898) and high-voltage therapy (introduced into this country by Reginald Morton), in the presence of X-ray and radium specialists who know more about the subjects than I do, I shall say nothing. Russ and Hector Colwell in "Radium, X-Rays, and the Living Cell," say:—

"In radiology applied to biological problems there is a double difficulty, for the intensity of the irradiation, be it X-ray or radium, is a quantity which under experimental conditions presents very considerable difficulties in its accuracy of measurement, and the animal itself represents a complex which refuses to be reduced to simple terms."

As regards heliotherapy—artificial sunlight—ultra-violet rays—"where the rainbow ends"—much has been done, much remains to be done, for this increasingly valuable method of treatment. The reaction of the skin to stimulation by electric energy wants further investigation, and, as Dr. Turrell aptly put it, "the skin has too long been regarded as a thing of sores and pimples."

Year by year electrology and radiology are proving more and more useful in all branches of medicine and surgery. In my opinion they would be of still greater value if all properly qualified electrologists and radiologists holding hospital appointments were regarded by the physicians and surgeons as learned colleagues and not merely as technicians!

The foregoing is a brief review of the immense advances made in every branch of medicine since my student days. Drinkwater, in his book entitled "Fifty Years of Medical Progress" (1873-1922), a book which I have found very useful in verifying my dates and data, gives a summary of progress of medical science and practice during the last half century, which he aptly describes as the golden age of medicine. Some of the junior members probably may think that our teachers in these bygone years must have been a very ignorant set. Such they were decidedly not, and their capabilities gave the lie direct to the jibe, uttered, I believe, by Bernard Shaw, that "Those who know—do! those who don't know—teach." They knew all that there was then to know, and they knew how to teach. They taught us to use our powers of observation, and whatever wits Nature had endowed us with.

Since those days there have been great advances in technique, but however great

these advances in technique, whether of electro-diagnosis, X-ray examination, biochemistry, or bacteriology, if we lose sight of the fundamental value of accurate clinical observation and common sense in the interpretation of the results acquired by such technical methods, all those advances will have gone for nothing. There is a tendency to-day for the student who cannot realize what these technical advances have meant to the men who in their early days groped for the truth about disease with little or no help, excepting that of their eyes, hands, and common sense—there is a tendency, I say, for the student to give technique in these matters a place much too near the forefront of his attention, and to relegate to a secondary position the old knowledge gained from men who, with all their limitations, recognized when a patient was ill, used all their powers to cure him, or, if that was not possible, to make him as comfortable as they could.

The tendency on the Continent, in general (and it shows signs of spreading to this country), is to regard a patient merely as a case—a scientific problem for investigation; and while this way of regarding things has its undoubted merits it is of little value in the hands of men not taught to look upon their patient as a human being, with a mind as well as a body, and an emotional side, with all its marked influence on his physical condition.

A man may have a mind stored with all the up-to-date facts of pathology, biochemistry or bacteriology; yet, if he forgets that our knowledge has not yet taken us up to the level of a complete understanding of that complex mass of unstable living material which makes up a human being, he will never, in the real sense of the word, be a master of the art as well as of the craft of medicine.

When he has learnt to respect the work of the great men of the medicine of the past, to retain the solid portions of their work (and there are many such) as form the enduring foundations of medicine; when he has learnt to realize that the mere collection of disjointed scientific facts does not endow him with the divine gift of healing nor with such powers as the ancient gods possessed, he will realize the truth of—

“Dis te minorem quod geris imperas.”¹

If all of us, in that most proper spirit of scientific humility, work steadily at our problems and practise what James Mackenzie called the law of progression, i.e., that the discovery of a fact should not be the end of the investigation but should be used for the discovery of other facts, then the results will be fit to hand on to our successors, who, in their turn, and in the same spirit, may achieve more.

I have spoken of many things which you already know, and of many other subjects than the particular branch of the noble art of healing to which we are all proud to belong, but we must remember that—

“The game is more than the players of the game,
And the ship is more than the crew.”

¹ “Thou rulest because thou holdest thyself lower than the gods.”



Section of Electro-Therapeutics.

President—Dr. ALASTAIR MACGREGOR.

Osteitis Deformans (Paget's Disease of Bone).

By R. E. ROBERTS, M.D., B.Sc., D.M.R.E.Liv., and
MORRIS J. COHEN, M.D.Liv., M.R.C.P.Lond.

HISTORICAL.

REGARDED in the light of history, it would appear that osteitis deformans is an ancient disease, for Jonathan Hutchinson found what seems to be a good example of the malady in a portion of a parietal bone removed from an Egyptian tomb. Furthermore, that ancient calvarium, known as the Neanderthal skull, is considered by Butlin to have belonged to a sufferer from this affection. In 1869 Wilks described a case of deformities of the bones, with subsequent post-mortem examination, and labelled it osteoporosis, or spongy hypertrophy of bones. This was afterwards recognized as an instance presenting the lesions described later by Paget. It was Czerny, in 1873, who first used the term "osteitis deformans" to describe a condition of deformity and softening of the tibia and fibula in a young soldier. But it was not until 1876 that a clear account of the disease was rendered by Sir James Paget, who made a study of five cases. To this lucid description very little has been added to the present day. In 1882, Paget added further observations on seven cases, and by 1889 he had made notes of twenty-three cases altogether. Von Recklinghausen, in 1891, described a disease of bones which he called "osteomyelitis fibrosa," and which is considered by many to be closely related, if not similar, to Paget's disease. Much has been written on the subject since Paget's communication; yet but little light has been thrown on the ætiology, and scarcely anything of value is known of useful treatment.

The disease is found in the white races of Europe and America. It has been recorded in Japan, and Stegmann has noted the affection in American Indians. American negroes are liable to it (e.g., two of Lewin's cases); but we have found no report of cases occurring amongst negroes in Africa.

Osteitis deformans has been noted in horses, and recently Corson-White had studied the disease in monkeys. The same writer mentions that Goldman described typical examples in fowls, that Jost knew of cases in monkeys and in a young lion, and that Rossweg found it in goats. In one of Corson White's monkeys so marked was the craving for lime that it would eat the plaster from the walls, when it could get at it.

Although more than 300 human cases have now been recorded, we are encouraged to add our series of sixteen cases to this large list.

In order to obviate repetition, the clinical and radiological features of Case I are given in greater detail, whilst in the others only the main points are mentioned.

DESCRIPTION OF CASES.

CASE I.

F. C. D., male, aged 42, watchman, noticed four years ago that right lower limb "began to go out of shape and to bend," and at the same time experienced aching pains in legs. The lateral curve of femur came first, then shins began to bend outwards, the left following the right side; and then kyphosis, with pain in lumbar region of the back and in occipital region of the head. Three years ago clavicles became prominent and chest protruded more forwards.

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A year later owing to pressure of cap on his temples he was obliged to buy larger sized head-gear. He has not noted any change in his hands or feet. The lower jaw to him "appears to have grown thinner." Eyesight "not as good as it used to be," but hearing is unaltered. Pain in limbs and back only on walking, slight on lying down, none at night. He is unmarried. One brother and two sisters alive and well; one sister died of "rheumatism and heart failure." As far as he knows no one in his family suffers from or has been affected with a condition at all approaching his own. No history of cancer, tuberculosis, or gout, in the family. When 9 years old, whilst wheeling a barrow full of coal he had "both legs broken." In 1918 he fell from a bicycle and fractured his right humerus. The fragments united well. He had pleurisy twenty years ago. Five years ago a polypus was removed from his right ear.

The head and face present a triangular appearance with chin as apex and forehead as base. Both eyes slant inwards and downwards. No arcus senilis. Pupils react to light and to accommodation. The face is small in comparison with the vault. The temporal arteries are not prominent. He believes that his forehead is larger than it used to be. Circumference of head is 23 in. The teeth have been lost gradually; altogether six stumps are left. Thyroid gland not palpable.

Chest shows marked kyphosis of whole of dorsal spine, which is rigid. Chest square, flattened bilaterally, and hence is deeper antero-posteriorly than from side to side. It is narrow above and broadens out below and on standing projects over abdomen. Sternum more prominent in its lower part. Clavicles are half as thick again as normal, with great accentuation of forward curve, but surfaces are smooth. No beading of ribs; and lower ribs are less oblique than normal. Percussion note resonant. Movements limited.

The abdomen is diamond-shaped, very short, but broad. Pelvis is wide, conforms to female type. Posteriorly, innominate bones are prominent and flare outwards. Iliac crests and anterior superior spines are about twice usual thickness. Lower ribs almost touch iliac crests. There is a deep transverse crease at umbilicus. Lordosis. No herniae.

In upper limbs no changes made out in the humeri. Both radii and ulnæ slightly curved and thickened, the curvature and thickening being more marked in the upper part. No changes in hands and wrists.

The lower limbs show femora curved forwards and outwards. Shafts thickened to twice the normal; smooth surfaces. No marked thickening at knee-joints, but there is creaking on movement, more marked in the right joint. Tibiæ are curved forwards and outwards, both curves being more accentuated than in the femora and more so on the right side. Usual edges and protuberances lost. Thickening is mainly in middle of the shaft. Surfaces of tibiæ are irregular. On standing, the shins overhang the feet, forming an acute angle in front. When lying in bed the posterior aspects of knees do not touch the bedclothes, the joint being raised several inches. The distance between the tibiæ below the knee-joints (with heels touching) is 18 in. Distance between the knee-joints is 11 in. Movements at the knee-joints good; at hip-joints flexion and extension good, abduction limited. Knee-jerks present.

His gait is slow, awkward, waddling, or like the rolling of a ship. He drops to the right owing to greater deformity on that side. The body is bent forwards and the head lies forward and down, and the back doubled up. He usually requires the support of a stick. The hands during walking reach down as far as the knees. The bowing of the legs is so extreme that the feet cross in front like a pair of caliper forceps.

Altogether, appearance is simian; the crouching, slow painful movements are more anthropoid than human. In walking, a dull ache is experienced in knee- and hip-joints, more so on the right side. He showed one of us (M. J. C.) a photograph taken in 1911, when he was in the Territorial Forces. He was then 5 ft. 7½ in. in height, and his appearance was that of a normal erect man. His present height is 5 ft. 2 in., and the distance between the tips of the middle fingers with arms outstretched is 5 ft. 10 in.

Wassermann reaction completely negative. Blood-pressure taken on several occasions showed the systolic at no time more than 125 mm. of mercury, and diastolic not more than 80 mm.

In the treatment, no material difference was noted after trying thymus gland (5 gr. t.d.s.), parathyroid (10 gr. t.d.s.) and calcium lactate (15 gr. t.d.s. in mixture), respectively. When last seen the condition was still progressing. So far the patient has found rest in bed alone sufficient to allay symptoms.

We have refrained from giving many measurements because the deformities are so obvious that the figures would scarcely serve a useful purpose.

Although presenting breadth and massiveness of bone in places double or treble the normal, his appearance is not that of strength, but rather of weakness, for the musculature is flabby. So much does his appearance tally in many respects with the original description of the disease by Paget, that on seeing the patient one could not help thinking of him as a vision in flesh and blood conjured up out of the famous surgeon's notes.

X-ray Appearances.

Skull.—Fig. 1. Looked at in profile, the skull is seen to be flattened from above downwards, showing a slight tendency to "mushrooming" on the vertebral column. The vault is thickened; its inner surface is clearly defined and smooth; its outer surface is ill defined and roughened by multiple projections and erosions, producing a blurred ragged contour.

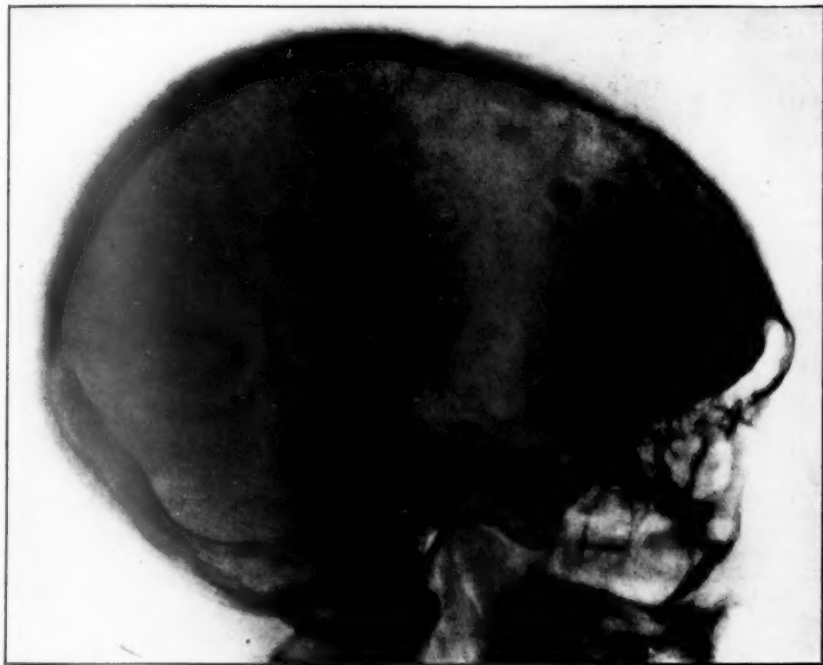


FIG. 1.—Paget's disease. Flattening. Inner table well defined. Outer table thickened and ragged. Islands of dense bone. (Calcified pineal body. Vertical posterior clinoid processes.)

There is no differentiation into inner and outer tables with intervening diploë. The general appearance of the bone is that of an amorphous or granular matrix with small irregular areas of increased translucency and opacity dotted about, the latter thus forming islands of dense bone. The vascular grooves are ill defined; the sutures are obliterated. The frontal sinuses are well defined; the basis cranii flattened; the posterior clinoid processes are prominent, and stand up vertically; the anterior clinoid processes are short. The distance between the anterior and posterior clinoid processes thus appears to be increased. The pituitary fossa itself appears to be within the normal limits as regards size.

Spine (dorsal and lumbar).—There is no malformation or flattening of the bodies of the vertebrae and no diminution of the intervertebral spacing as seen antero-posteriorly. The

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bodies of the vertebræ show an amorphous granular appearance with coarse trabeculæ, chiefly in a vertical direction, though some horizontal trabeculæ are seen near their upper and lower surfaces.

Pelvis.—The bones of the pelvis look massive, but evidently are, or have been, soft, as the inlet has become deformed, and presents a triangular shape; the indentation is greater on the left side than on the right. The outline of the brim is fairly clearly defined, but in places shows a double shadow. The bones show on the whole a granular appearance with, in places, a tendency to coarse trabeculation, but even the trabeculæ are blurred. The iliac bones are splayed out; they show irregular areas of translucency and a good deal of coarse striation. On the right side the pubic ramus shows a differentiation into cortex and medulla; on the left side there is no such differentiation visible, and the bones here show a considerable thickening.

Long Bones.—Many of the bones (both femora, both tibiæ, both fibulæ, both radii and ulnæ) show bending, producing an exaggeration of the normal curves. The humerus shows no bending. In the upper part of these bones (including the humerus) there is seen a general thickening, which more particularly involves the cortex. The outline of the bone is for the most part rough. In some cases (femora, humeri, ulnæ) the outline is well defined; in others, especially the anterior borders of the tibiæ, it is blurred.

In all the bones except the right tibia, the cortex has an amorphous appearance, with just a few coarse striæ, but in the right tibia (fig. 5, p. 20), these striæ are well marked, passing vertically down through the anterior cortical layer, parallel to the surface; the medullary strands present a criss-cross pattern, the cortical strands are longitudinal. (It is possible that the so-called "medullary" strands are really cortical strands seen through the more translucent medulla.) In the left femur, as the striæ become more clearly defined in the lower part, there is a gradually increasing lack of differentiation between cortex and medulla.

Small elongated translucent areas, suggestive of cysts, appear in most of the bones.

The right humerus shows well defined trabeculation, coarse strands running more or less longitudinally. An old united fracture of the middle third is shown, through which the longitudinal strands can be traced. The differentiation into cortex and medulla in the upper half is lost. (The trabeculæ are better defined in the radiograph of February 20, 1925, than in that of March 19, 1924.)

In the hands and feet no bone changes are shown.

CASE II.

P. R., male, aged 67, noticed bowing of his left leg four years ago. Two years later he "hurt his left knee," and since then bending and thickening of the left tibia have become more obvious. He has not noticed his head growing bigger. He has suffered from "rheumatic" pains in the legs for some years past. An accident to his left eye in 1882 destroyed the vision in that eye. No one in his family has ever had a similar condition of the bones. Wassermann reaction completely negative. Blood-pressures: systolic, 135 mm., and diastolic, 90 mm. of mercury. There are locomotor brachials.

The general aspect of head tends to be triangular, with the vault as base. The forehead is large and prominent, and there are two large frontal bosses. The skull is broad. Tortuous, thickened, temporal arteries are very evident. Circumference of head is 23½ in.

The chest is somewhat kyphotic. No changes in clavicles, or marked alteration of contour of chest wall. With exception of a double inguinal hernia there are no lesions calling for attention in the abdomen.

In the upper limbs no evident abnormality made out.

The left tibia is bent forwards and outwards, more markedly in its upper part. It is half as thick again as normal. The left foot is flat, and the left shin overhangs it slightly. The circumference of the left calf is 14½ in.; right calf 13½ in. Distance between the knee-joints is 3½ in. Left knee thickened, movements good. Left femur slightly curved and thickened, noticeably at the lower end. Right lower limb, no abnormality seen.

Gait shows tendency to waddling; arms dropped, head drooping, back bent.

X-ray Appearances.

Skull.—(Fig. 2.) The inner surface of the calvarium is not so clearly defined as in Case I. The vault is thickened, though to a less extent than in Case I. The small opaque areas are smaller and more numerous than in Case I, and give an impression of multiple tufts of opaque cotton wool stuck to the surface of the skull. The vascular grooves and channels are fairly distinct and not appreciably broadened. In the upper fronto-parietal region on the right side

there is a small circumscribed translucent area which gives the appearance of a hole in the vault. The frontal sinuses are well defined and the sella turcica is approximately normal in size and shape.

Spine.—The lumbar spine shows evidence of chronic osteo-arthritis. There is no apparent trabeculation of the bodies of the vertebrae.

Pelvis.—The iliac bones are splayed out and show an irregular thickening of their crests. The outline of the pelvic bones is not very clearly defined. Coarse, irregular striation is seen in the medullary portion of the bones; the cortex is thickened. The pelvic cavity shows a deformity due to pressure. The sacro-iliac joints are indistinct. The iliac arteries are seen to be calcified.



FIG. 2.—Inner table not markedly involved. Numerous dense tufts and patches with intervening translucent areas.

Long Bones.—The bending of the long bones with the exception of the left tibia is not so marked as in Case I. The right femur and the left tibia show a mortar-like thickening of the cortex with little or no indication of trabeculation. Their outline is rough and irregular but on the whole it is fairly well defined. On the outer side of the right femur are three small incomplete transverse fractures. In the anterior convex border of the left tibia (fig. 8, p. 24) there can be counted twenty small incomplete fractures, at right angles to the surface of the bone. These apparently only affect the cortex of the bone along the shin. Individually they resemble, in the skiagram, the screw-holes left in a bone when a fracture-plate has been removed. In the great trochanter of the right femur there is a rarefaction of the bone

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whilst the neck shows a slight degree of coxa vara deformity. Both knee-joints show osteo-arthritic changes. Both ankle-joints show well marked osteo-arthritic changes and on both sides the os calcis shows bony spurs on the upper and lower surfaces of the heel. Many of the joints of the hands show slight changes of chronic osteo-arthritis. The middle metacarpal bone of the right hand shows a slight thickening of the cortex.

CASE III.

S. D., female, aged 53, has been complaining of pain in the left hip and lower part of the spine for nine months, when it first began "in the small of the back." She has experience



FIG. 3.—Marked changes involving both inner and outer tables and base. Flattening and gross irregularly calcified thickening of calvarium.

difficulty in walking for three years. Six months ago legs began to cross. Has had "dizzy bouts" in the head for last two years. Has not noticed head growing bigger. Had swellings and abscesses round knee-joints when about seventeen years old. Could move joints completely without pain at that time. She is married and has one child (now twenty-five years old); no miscarriages.

Wassermann reaction strongly positive (Thompson-Yates Laboratories). General condition fair. Heart not enlarged, but there is a soft blowing, systolic localized murmur at the apex. Pulse is of good volume and regular in time and force. Blood-pressures, systolic 165 mm. of mercury, diastolic 100 mm.

Head: vault is large but has smooth, uniform surface. Brow is prominent. In comparison the face is small. The temporal arteries are tortuous, thick and hard.

Chest tends to be square. Clavicles are greatly thickened, curves accentuated. On standing, there is marked kyphosis of whole dorsal spine, with stiffness of movements.

Abdomen short and full. The last ribs almost touch iliac crests. There is a transverse crease or furrow passing through the umbilicus. Some lordosis. Iliac crests thickened, and flare outwards.

No pathological changes evident in upper limbs.

In the lower limbs there are multiple, thin, papery scars above and below knee-joints, some of them adherent to bone. The scars are more numerous at the upper end of the tibia where there is a nodular thickening of the bone. Femora are thickened to about twice normal, especially lower portion of the right femur. In the middle of the inner group of the



FIG. 4.—Triangular deformity of pelvis. Coarse, fluffy trabeculation in pelvis and femur. Coxa vara and bowing of femora.

left hamstrings there is a hard spindle-shaped swelling of unascertained nature, adherent to skin in one place, and not opaque to X-rays. Left leg slightly everted. Movements of both knee-joints complete. Right hip flexes to only 90° ; abduction completely absent without movement of pelvis. No rotation possible.

Gait difficult and laboured. Head drooping and held down. She says "sometimes I have to bend nearly in two." Limbs cross; progress slow. Does not use sticks in walking. But in the street holds on to railings or fence or touches walls and lamp-posts. At home she obtains support from the walls and furniture.

X-ray Appearances.

Skull (fig. 3).—Skull flattened. Gross thickening of the calvarium is seen. Inner and outer tables indistinguishable from the diploë. Inner and outer surfaces of the bone rough, woolly and ill-defined all over the vertex. Irregular areas of translucency are seen. The

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vascular grooves are not distinguishable, and the sutures are ill-defined; the pituitary fossa is approximately normal in size but ill-defined. The base shows a thickening and mortar-like texture of the bone, and is slightly flattened.

Pelvis (fig. 4, p. 19).—Iliac bones splayed out. The pelvic cavity is triangular in shape, due to deformity from pressure of the heads of the femora on the softened bones. The structure of the bones of the pelvis is ill-defined and blurred. No differentiation between cortex and medulla. The general appearance is that of a coarse, blurred trabeculation on a granular or mortar-like background.



FIG. 5.—Bowling of tibia and fibula. Thickening and longitudinal trabeculation in cortex of tibia (upper half). Criss-cross striæ (? cortical) seen in (or through) medulla.

Long Bones.—The upper-thirds of both femora show gross thickening of the shafts; there is a coxa vara deformity, the trochanters being almost in contact with the iliac bones. The outline of the bones is blurred. The cortex is much thickened; there is no clear differentiation between cortex and medulla. There is coarse, blurred trabeculation in a rather irregular manner throughout the shafts of the bones. The middle and lower thirds of the femora show a thickening of the cortex, with longitudinal striæ. Small translucent areas are seen in the cortex which are presumably cysts; some of these are very long. Outline of the bones clear cut, but rough

The tibia shows a thickening of its upper third, and an elongated translucent area is seen in its anterior cortex (? cyst). There is a lack of differentiation into cortex and medulla in the anterior part. Very little trabeculation is seen in the tibia.

The lower end of the radius shows a thickening, and the differentiation into cortex and medulla is lost.

CASE IV.

J. R., male, aged 36, noticed swelling of the right leg below the knee-joint fourteen years ago. The swelling has gradually increased in size since then, but no pain was experienced till about four years ago. There is now a diffuse, hard swelling of the upper end of the right tibia.



FIG. 6.—Cyst in cortex of upper end of tibia (see fig. 5). Calcareous arteries.

The knee-joint is swollen and stiff, and is kept in a semiflexed position. Patient suffers from cramping pain behind the knee which is worse at night; there is no pain actually in the bone. No deformity of the spine or other limbs seen. He has never complained of headaches.

X-ray Appearances (January, 1924).

Skull.—Skull flattened; calvarium thickened, especially posteriorly. Inner table, diploë and outer table show no relative differentiation; outer table has lost its clarity of outline and shows a fluffy, indefinite contour with irregular ill defined areas of translucency. Inner surface moderately well defined. The whole of the calvarium shows irregularly distributed areas of alternate opacity and translucency merging into each other.

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Frontal sinuses ill defined; sutures obliterated.

Vascular grooves fairly well defined in anterior half, ill defined in posterior half. Sella turcica approximately normal in size and shape.

Spine.—The bodies of the vertebræ show a tendency to coarse irregular striation. In the transverse processes of the fifth lumbar vertebræ there is a well marked horizontal striation. The bodies appear to be flattened and are relatively broad. Sacrum shows well marked criss-cross trabeculation. Sacro-iliac joints indistinct, especially in their upper parts.

Pelvis.—Pelvis is massive looking, but the outline of the bones is somewhat blurred. Slight deformity of shape of the inlet.



FIG. 7.—Same case as fig. 5 three years later. Note longitudinal trabeculation through previously cystic area in anterior part of upper end of tibia. Longitudinal trabeculation in lower end of femur. Osteo-arthritis of knee-joint.

The iliac bones show a coarse striation chiefly in two directions: (1) radial; (2) concentric (parallel to the crest). The appearances are symmetrical. The ischium shows a coarse striation chiefly at right angles to the surface and extending into the cortex (cf. Case II). In the ischium the central part of the bone is more opaque than the periphery.

Long bones.—The right humerus shows a thickening of its upper two thirds; differentiation

into cortex and medulla is lost, and the bone is denser in its central portion than at the periphery. Longitudinal striation is seen, with elongated translucent areas in the cortex suggestive of cysts.

The right femur in its neck and upper third shows a massive thickening. The appearance is that of coarse trabeculation on a mortar-like basis. The trabeculae roughly correspond to the lamellae of normal bone. In its middle third the thickness is that of a normal bone but there is a granular appearance. In its lower third the bone is again thickened. The central part of the bone is much denser than the periphery, the cortex being thickened and translucent. A few longitudinal striae with intervening translucent areas are seen.

Right knee-joint shows bone changes of chronic osteo-arthritis.

The right tibia (fig. 7) in its upper half shows a gross thickening with increased translucency of the periphery. Coarse longitudinal striation and translucent areas are seen, especially in the anterior portion. These striae are absent in a previous radiograph (taken on January 22, 1921) but well defined in the radiograph of January 30, 1924.

The left femur and tibia show changes which suggest that the bones are in the early stage of the condition seen in the right leg; definite longitudinal striae are seen, especially in the upper end of the tibia.

Appearances of the Right Knee of J. R. in January, 1921 (fig. 6).

The changes then seen consisted chiefly of a thickening or expansion of the anterior cortical layer at the upper third of the tibia. Of this area the upper half showed irregular ill-defined projections on the surface, whilst the lower half showed a translucent area with a well defined thin layer of bone over its surface. The appearance of this portion of the bone suggests a cyst. The longitudinal trabeculation seen in the radiographs taken three years later is not present, or at any rate to any appreciable degree, in the earlier radiograph; and the general appearance of the bone is more granular.

The femur also showed more granulation and less trabeculation in the earlier radiograph.

CASE V.

A. F., male, aged 69, has suffered from pain in the right hip on and off for eight years; during the past three months this has become more severe. He also suffers from pain and stiffness of the right knee. There is no visible deformity of the back, and no increase in the size of the head has been noticed. The legs show slight bowing, and there is some thickening about the lower part of the right forearm.

X-ray Appearances.

Skull.—Skull flattened; shows a thickening of the calvarium especially posteriorly. Outline fairly clearly defined and inner and outer tables distinguishable. Sutures obliterated; vascular grooves indistinct. Areas of increased opacity and translucency are seen; frontal sinuses well defined; pituitary fossa approximately normal in size.

Spine.—The bodies of the vertebrae present a "woolly" appearance with slight trabeculation. Slight osteo-arthritic changes present.

Pelvis.—Pelvis deformed, the inlet being triangular in shape. The bones present a granular appearance with a few coarse striae.

Long Bones.—The articular surfaces of the hip-joints show a close approximation indicating a cartilaginous erosion from chronic arthritis. A bilateral coxa vara deformity is present with slight bowing of both femora. The left femur shows an irregular thickening of the cortex with coarse striae running more or less longitudinally down it. The right femur at its lower end shows a blurring of its outline and there is evidence of chronic arthritis of the right knee-joint.

The right radius and ulna (fig. 9) show thickening, with an "S" shaped bend in the radius. The radius shows coarse longitudinal striae and its contour is ragged and wavy.

Cortical thickening and homogeneous increased opacity is seen in the metacarpal of the fourth finger and in the proximal phalanx of the little finger of the right hand and in the ulna. The index metacarpal shows similar, but much slighter, changes.



FIG. 8.

FIG. 8.—Bowed tibia showing twenty incomplete fractures of anterior border. Granular or amorphous type of bone change.



FIG. 9.

FIG. 9.—Granular thickening of cortex of ulna and of fourth metacarpal and fifth proximal phalanx. Thickened radius with "crumpled" inner border and longitudinal trabeculation in outer border.

CASE VI.

M. W., female, aged 45, during the past six months has suffered from pains in muscles of the left leg, thought to be due to fibrositis. When walking quietly, experienced a spontaneous fracture of the left thigh. Clinically, nothing to suggest Paget's disease.

X-ray Appearances.

Left Femur (a few days after the fracture).—The lower half of the left femur showed irregular thickening with a fracture three inches above the knee-joint. The bone presented a granular appearance with a suggestion of very faint coarse trabeculae. The upper half of the tibia showed a thinning of the cortex with increased translucency of the medulla. The knee-joint showed evidence of chronic osteo-arthritis.

(Subsequent union of the fracture took place. When the union was complete, clearly defined irregular trabeculae were shown in the radiograph running longitudinally up to and through the site of the fracture.)

Skull.—The skull was not radiographed till two years after the fracture had taken place. It then showed a flattening and loss of clarity of outline of the vault. In a radiograph taken

one and a half years later the skull changes had disappeared and the bone now showed normal X-ray appearances.

(It is interesting to compare the horizontal and vertical measurements of the skull on these two occasions. In the first radiograph the ratio of horizontal to vertical measurements was $212 : 151 = 1.40$; in the second radiograph it was $201 : 148 = 1.36$; i.e., at the time when the pathological changes were demonstrable in the radiograph, and when the skull was presumably comparatively soft, the ratio of the horizontal measurements to the vertical was greater than when these changes had disappeared and the skull had recovered its normal radiological appearances. In other words, as recalcification took place, the skull returned to a more normal shape.)

Other Bones (spine, pelvis).—No bone change was shown in these parts at any time.

CASE VII.

T. B., male, aged 70, has suffered from "rheumatism" on and off for several years. During the past three weeks has had severe pain in the region of the hip and ankle, increased by walking. Slight bowing of both legs, especially the left. Three weeks after admission to hospital he twisted his left leg and fractured the upper end of the shaft of the left femur.

X-ray Appearances.

Skull.—No flattening and no thickening of the calvarium. Inner and outer tables distinguishable and outline clear cut. Irregular areas of increased density and translucency are seen.

Spine.—The vertebræ present a woolly granular appearance but there is no definite striation visible. Chronic osteo-arthritis changes present.

Pelvis.—No obvious deformity. The bone shows a faint coarse striation; irregular areas of translucency are seen especially in the ischium.

Long Bones.—The head and neck of both femora show faint coarse blurred striæ, and the cortex of the shaft is thickened. Both femora, especially the left, show a bending of the shaft, and 2 in. below the great trochanter of the left femur a recent fracture is seen.

The left tibia shows a bending (convex forward), thickening of the cortex, and faint longitudinal striation. In the right tibia no bone-change is shown.

CASE VIII.

M. B., male, aged 46, stated that up till about sixteen months ago he had been a very strong man and never away from his work. He was then crushed in a coal-pit and was confined to bed for six weeks. Since that time he has complained of steadily increasing weakness. His appearances now suggest typically the deformities of Paget's disease—the head is large, the back bent and the legs bowed.

Skull.—The skull shows flattening, irregular thickening of the cortex and irregular areas of translucency and opacity. Pituitary fossa appears normal.

Spine.—The vertebral bodies show faint vertical striation.

Pelvis.—Pelvis deformed, being flattened from below upwards. Marked fine trabeculation seen throughout the pelvis with multiple areas of increased translucency.

Long Bones.—Femora show thickening and coarse trabeculation.

In the lower end of the right tibia there is evidence of trabeculation. The arteries being calcified show up very clearly. In the right os calcis there is seen to be an accentuation of the normal lamellation.

CASE IX.

W. H. G., male, ten years ago noticed "rheumatic" pains in left ankles, later extending to the left knee, right knee and right ankle; relieved by rest. Six years ago pains in head; noticed that head was enlarging (hats $6\frac{3}{4}$ to $7\frac{1}{2}$) and that left tibia was becoming bowed.

During the past one and half years has suffered from shooting and cramping pains in the muscles of the calves and thighs.

No spinal deformity. Early tabes and chronic malaria. Clinical and radiological evidence of duodenal ulcer (this was subsequently confirmed by operation).

X-ray Appearances.

Skull.—Calvarium shows slight thickening but no flattening; inner surface clear cut; outer surface less distinct and of irregular contour. Areas of increased translucency and opacity are seen. The pituitary fossa appears to be slightly enlarged.

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Pelvis.—Shows very slight deformity. Presents a dense granular appearance without any evidence of striation.

Long Bones.—Upper ends of femora show slight thickening of the cortex, which exhibits a more or less homogeneous granular appearance without striae. The left tibia shows a bending in its middle and lower thirds, convexity forward. The cortex of this part is thickened, and shows coarse irregular striation. The cortex of the left os calcis shows a granular thickening at the expense of the cancellous tissue. Right radius shows thickening and increased opacity with more translucent patches. Appearance granular without striation. Right thumb metacarpal shows increase of opacity.

CASE X.

M. L., female, aged 59, fell two months ago, fracturing her right femur. Clinically, there is nothing to suggest Paget's disease.

X-ray Appearances.

Skull.—Shows thickening of the calvarium, the outline of which is smooth. The appearance of the bone is more or less homogeneous with one or two more opaque patches posteriorly. Sutures obliterated, the vascular grooves faint, and the frontal sinuses well marked. The pituitary fossa appears to be normal in size.

Lumbar Spine.—Except for the presence of chronic osteo-arthritis no bone changes are shown.

Pelvis.—No deformity of pelvic cavity. The general appearance is that of a granular or amorphous opacity with a few more translucent areas. No striation present.

Long Bones.—Upper part of each femur shows a thickening of the cortex, the general appearance being an amorphous granular opacity with a few faint coarse striae. Two inches below the lesser trochanter of the right femur there is a transverse fracture. Left knee-joint shows chronic osteo-arthritic changes; right knee-joint shows no such changes. In the right humerus no bone change is shown.

CASE XI.

H. E., male, aged 60, has suffered from increasing weakness and vague pains. Up to nine years ago he was quite straight; since then the legs and back have become more and more bent. He noticed enlargement of the head four years ago. He now shows typical deformity of Paget's disease.

X-ray Appearances.

Skull.—Shows flattening, with marked ragged thickening of the calvarium. Both inner and outer surfaces indistinct, especially the latter, which shows great irregularity of contour. The outline resembles that of the "woolly head of a piccaninny." Sutures obliterated; vascular grooves very indistinct. Pituitary fossa ill defined but apparently normal in size.

Pelvis and Long Bones.—Innominate bone, head and neck of the femur, show cortical thickening, and coarse, faint trabeculation. There is evidence of chronic arthritis of the hip-joint and slight coxa vara deformity. No bowing of the right tibia. The upper two-thirds shows thickening with very faint striation in the upper part. Right radius and ulna show cortical thickening, with very faint longitudinal striation, but no bending.

CASE XII.

M. S., female, aged 57, complains of weakness, loss of weight, and rise in evening temperatures. Has albuminuria, and was sent for X-ray examination of the urinary stone area. In the radiographs bone changes of osteitis deformans were observed in the pelvis and spine. On being questioned, patient stated that for the past four or five years she had noticed that her head was increasing in size; six months ago she noticed that her left leg was bending.

X-ray Appearances.

Skull.—The whole calvarium is greatly thickened. Outline of inner surface is in part well defined, and in part indistinct, especially posteriorly. Outer surface pitted and very rough. The whole surface of the bone shows numerous small areas of opacity, presumably corresponding to the elevated portions, the pitted portions being more translucent. Skull shows a slight flattening. Sutures are obliterated and vascular grooves very faint. The pituitary fossa indistinct, but appears to be enlarged.

Spine.—Lumbar spine shows well-marked vertical trabeculation of the vertebral bodies, with horizontal striation of the adjacent surfaces.

Pelvis.—The pelvic cavity shows deformity, its shape being roughly triangular; the deformity is greater on the right side than on the left. Between the trabeculae more translucent areas are seen.

Long Bones.—Head and neck of both femora, especially the right, show a coarse, clear-cut trabeculation, the striae being along the lines of the normal lamellae. Lower ends of both femora show thickening and trabeculation. Middle portions show no bone changes. Right knee-joint shows bone changes of chronic osteo-arthritis. Upper end of left tibia shows thickening of the cortex with trabeculation. No such change is seen in right tibia.

CASE XIII.

F. B., female, aged 66, a sister of M. S., noticed bowing of the legs about seven to eight weeks ago, followed by pains in the knees.

X-ray Appearances.

Skull.—No bone change shown.

Pelvis.—No deformity. General appearance granular with faint striation. Ischium on left side thickened and shows small translucent areas.

Long Bones.—Coarse striation seen in the lower ends of both femora. Appearances of the rest of the bone normal. Evidence of chronic osteo-arthritis of the right knee-joint. Upper ends of both tibiae, especially of the right one show thickening of cortex with striation. Right tibia shows slight bending, convex forwards.

CASE XIV.

J. F., male, aged 58. Sent for X-ray examination of skull because of choroiditis and retinal hemorrhages. Patient gave a history of a fall from a ladder on to the head fifteen years ago; since that time he has noticed that his head has gradually increased in size (hats 6½ to 7½). One year ago vision began to fail and has become gradually worse. Complains of some stiffness in lower limbs; left tibia swollen.

X-ray Appearances.

Skull.—Flattening of vault and marked thickening of calvarium. Inner surface fairly distinct; outer surface ill-defined and presenting a ragged wavy contour. Pituitary fossa enlarged and the posterior clinoid processes throw an incomplete shadow suggesting either destruction or decalcification of their base. The sutures are obliterated and vascular grooves very indistinct. Frontal sinuses small.

Pelvis.—Deformity of inlet especially on the left side. Spreading out of iliac bones, thickening, especially of the left ischium. Amorphous appearances of structure with very faint striae.

Long Bones.—Upper and lower ends of both femora show faint coarse striation. Shaft of left femur shows some cortical thickening.

CASE XV.

J. L., male, aged 55. Rheumatism off and on for many years. Pains in arms, shoulders and knees, two years. "Neuritis" in the left arm six years ago. Stiffness in all joints. Slight bowing of both tibiae present; duration unknown. Breathlessness.

X-ray Appearances.

Skull.—Slight flattening of vault, with thickening of whole calvarium. Inner surface fairly distinct, outer surface not so clearly defined, and roughened. Multiple islands of increased density throughout surface with more translucent surrounding areas. Sutures obliterated, vascular grooves indistinct. Pituitary fossa ill-defined. Frontal sinuses very large with thin anterior wall.

Spine.—Vertebral bodies flattened, of indistinct outline, and showing slight trabeculation. Chronic osteo-arthritis of lumbar spine.

Pelvis.—Symmetrical deformity of pelvic cavity. Fairly well defined trabeculation of all parts. Calcareous gland shadows seen.

Long Bones.—Femora (upper part) show no bone change. Both tibiae show slight bending (convexity forwards). Upper half of both tibiae show granular thickening of cortex in anterior part, but thickened part is less opaque than remainder of cortex. Lower half of left tibia shows generalized thickening of cortex with diminished opacity. At extreme lower end, slight coarse striation. Right astragalus and left os calcis show slight coarse trabeculation. Right ulna shows thickening of upper half with bending, convexity backwards and inwards.

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CASE XVI.

A. R., male, aged 57. Typhoid eleven years ago. Swelling and pain in right leg past five years, especially of ankle-joint. No other symptoms. Slight bending of right tibia.

X-ray Appearances.

Skull.—No obvious flattening. Generalized thickening of calvarium. No dense islands. Sutures obliterated. Vascular grooves distinct and appear to be deep. Frontal sinuses of normal size but very thick anterior wall. Pituitary fossa not clearly seen.

Spine.—Lower lumbar spine shows granular or amorphous appearance of bone. No trabeculation.

Pelvis.—No deformity of pelvic cavity. Fairly well defined in outline. General amorphous appearance with slight coarse trabeculation in iliac bones. Small areas of increased translucency in pubis and ischium. Sacro-iliac joint ill defined.

Long Bones.—Both femora show coxa vara deformity with thickening of shafts; amorphous appearance of thickened cortex with faint coarse trabeculation of part next to medulla. Slight bending of right tibia with amorphous thickening of anterior cortex in upper half. No bone change in right radius, ulna or hand.

INCIDENCE.

The incidence as gauged from figures is not altogether reliable. Early cases are often missed. In considering statistics due allowance must be made for the frequency of X-ray examinations made at the institution, and also for the age of the patients admitted, and the function of the institution. As an illustration (mainly on the latter point), at Clifton Springs Sanatorium (U.S.A.), which is a hospital for chronic ailments, the incidence is roughly one in 3,000, whereas in general hospitals it is found seldom above one in 10,000. In Table I are a few figures to show incidence.

TABLE I.

Author	Hospital	Case	Admissions	Ratio
Hurwitz	Johns Hopkins, Baltimore	3	30,000	1 in 10,000
Da Costa	Jefferson, Philadelphia	3	38,000	1 in 12,666
Cutler	Massachusetts	7	285,000	1 in 40,714
Carmen and Carrick	Mayo Clinic, Rochester	15	237,000	1 in 15,800
Munford	Clifton Springs Sanatorium	4	10,558	1 in 2,640

ÆTIOLOGY.

The ætiology and pathogenesis of osteitis deformans are still shrouded in mystery.

Paget's view was that the disease is an inflammation of bone. Many still hold this to be the case. More recently authors have come to consider it an endocrine disturbance, and the gland chiefly blamed is the parathyroid. Some of the generally stated ætiological factors are more or less of historical interest. Jefferson suggests that osteomalacia is the acute form of the disease in which osteitis deformans is the chronic representation. Lawford Knaggs holds the disease to be caused by a toxin which may exist in many individuals, but to which only a small portion show an idiosyncrasy. He believes that the toxin is the same for osteomalacia, osteitis fibrosa, and osteitis deformans. In such cases, if resistance is very poor, osteomalacia may develop; if it is good in youth, osteitis fibrosa is staved off, and if toxin be still active at the senile period osteitis deformans may develop. The list of factors given as causative agents in the disease is the following: gout, rheumatism, bacterial infection and trauma, malignant disease, endocrine disorders, syphilis, trophic nervous disorders, heredity and developmental factors, arteriosclerosis, perverted metabolism. Objections can be raised to nearly all. For instance, gout, rheumatism, and arteriosclerosis are common, whereas Paget's disease is rare. Again, the majority of the sufferers yield a negative Wassermann reaction, nor do they react to antisyphilitic treatment.

Two of our cases had a positive Wassermann reaction.

There is a possibility that hereditary influence is greater than is generally conceded.

Thus Paget says:—

"I have tried in vain to trace any inherited tendencies to the disease. I have not known it in two members of the same family. Many have had gouty ancestors, but I do not think more than the equal number of persons in the same rank in life."

It is, of course, possible that the environmental factor in related cases plays some part, the individuals being exposed to the same influences if living together. Since the time of Paget's publications cases in which several of a family have suffered from the disease have now and again been recorded. There is no report of the condition noted in more than two generations. In Table II we give a few of the instances noted in the literature.

TABLE II.

Author	Relationship	References
Manwaring-White ...	Two brothers ...	<i>Brit. Med. Journ.</i> , 1909, ii, pp. 12-15.
Pick ...	Father and daughter ...	<i>Lancet</i> , 1883, ii, p. 1125.
Stahl ...	Two sisters ...	<i>Amer. Journ. Med. Sci.</i> , 1912, cxliii, p. 527.
Cettinger and Lafont ...	Father and two sons ...	Cited by Hurwitz (<i>vide infra</i>).
Smith ...	Father and son ...	<i>Med. Soc. Trans.</i> , Lond., 1905, xxvii, p. 324.
Chaufard ...	Mother and daughter ...	Cited by Fitz, <i>Trans. Assoc. Amer. Phys.</i> , 1902, xvii, p. 398.
Higbee and Ellis ...	Mother and son ...	<i>Journ. Med. Research</i> , Boston, 1911, xxiv, p. 43.
Lunn ...	Two brothers ...	<i>St. Thomas' Hosp. Rep.</i> , Lond., 1883-1884, xiii, p. 43.
Parry ...	Two sisters ...	<i>Brit. Med. Journ.</i> , 1912, i, p. 879.
Berger ...	Mother and son ...	Cited by Lannelongue, <i>Bull. Acad. de Méd.</i> , Paris, 1903, xlix, p. 299.
Kilner ...	Brother and sister ...	<i>Lancet</i> , 1904, i, p. 221.
Hurwitz ...	Mother and son ...	<i>Johns Hop. Hosp. Bull.</i> , 1913, xxiv, p. 266.
Abbe ...	Two brothers ...	<i>Journ. Amer. Med. Assoc.</i> , lxx, p. 371.

In our series two of the cases were sisters.

Comparatively few cases have been noted in which the ductless glands were diseased, but in those that have been recorded the gland mostly affected seems to be the parathyroid body. Cases of parathyroid hyperplasia without bone changes have been recorded. Erdheim believes that changes in the parathyroids are not the cause of bone changes, but the consequence of hyperfunction owing to increased calcium metabolism (Dawson and Struthers). We know of no instances of Paget's disease in which tetany has occurred.

Noël Paton has shown that one function of the parathyroid bodies is to prevent the formation of undue amounts of guanidine in the body. Their other function is to control calcium metabolism. Is it possible that the parathyroids assume a double function: (1) To help fixation of calcium by the osseous tissues; (2) to prevent the other tissues from taking it up? Once these functions fail, it may be readily expected that the osseous tissues can no longer fix the calcium, and the other tissues in the body easily take it up. This is the case in certain post-mortem records of Paget's disease in which, although the bones were deficient in hardness, other organs, e.g., lungs, stomach, arteries, spleen, pituitary, &c., presented a diffuse calcinosis. Some evidence of endocrine disturbance in osteitis deformans and other bone lesions as gathered from the literature is given in Table III.

TABLE III.

Author	Cases	Endocrine disorder
Higbee and Ellis ...	One case osteitis deformans ...	No parathyroids found, but islets of parathyroid tissue in the thyroid, which was itself fibrous
Dawson and Struthers ...	One case osteitis fibrosa ...	Simple papillary adenoma of parathyroids
Harbitz ...	One case osteomalacia ...	Adenoma of parathyroid
Jenkins ...	Nine cases osteitis deformans ...	One case had acromegaly, two others showed enlargement of sella turcica
Askanaazy, quoted by Harbitz ...	One case osteitis deformans ...	Tumour of parathyroid

AGE AND SEX.

Age.—In many instances patients consult the physician years after onset. Stilling records a case first seen at the age of 92, and an instance is also noted where the patient was first seen at age of 21 Czerny's case was that of a young man

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of 22. Generally patients are seen between ages of 30 and 50. In our series five patients were between 60 and 70 years of age, seven between 50 and 60, three between 40 and 50, and one below 40 years. The youngest was 36 and the oldest 70.

The onset of Paget's disease appears to be so insidious that it is difficult to obtain any reliable data as to age of onset. As far as could be made out from an interrogation of our patients, signs or symptoms compatible with the disease attracted the attention of the patient or his friends at the following ages: in six cases between the ages of 40 and 50, in five cases between 50 and 60, in three cases between 60 and 70, while in only two cases did they appear before the age of 40, the earliest being 22 years.

Lewin notes that examples of the disease have been seen to begin in tender years, at ages 12 (Elswer), 16 (Jones), 13 (Thibierge), 15 (Hartmann). It is possible that such cases are syphilitic in origin. In that respect it is of interest to cite Parkes Weber, who reports a case of a boy aged 14 with enormous enlargement of the bones of both legs and to a lesser degree of both ulnæ. The boy looked as if his legs below the knees were too long (as well as too thick) in comparison with his thighs and the rest of his body. Family history negative; gummata appeared later.

Weber drew up points of differentiation between osteitis deformans of congenital syphilis and Paget's disease. He cites similar cases noted by Dr. Porter Parkinson, J. Basil Hall, Hans Lorenz, and Fritz Spieler.

Sex.—As far as records show, sex incidence is about equal; perhaps it has been noted a little more frequently in males. In our series eleven patients were males, five females. In the family histories little light of a possible causative factor can be thrown on the subject.

PATHOLOGY.

All our cases are alive, and no opportunity offered itself for microscopical examination of affected bones. As yet, few cases are on record in which a necropsy was performed. Generally the findings have been fairly uniform, differences possibly being accounted for by the different stage reached by the disease.

The condition affects the osseous system generally, the order of frequency of bones mainly affected being the skull, tibia, femur, pelvis, spine, clavicles, ribs, radius, ulna, humerus. It may begin in one bone, the rest being afterwards affected; or, what is most probably correct, one bone is more noticeably affected than the others. Herbert French noted a case in which a tibia showed disease for six years before it was apparent in other bones. It is possible that where the disease is confined to a single bone, trauma is a factor of greater import than in the generalized form.

The periosteum is injected and adherent in places. On section the bone is irregularly spongy and soft, but is of ivory hardness here and there. Distinction between diploë and outer and inner tables of the skull may be lost. In advanced cases the medullary cavity is obliterated by coarse, irregularly-formed osteoid tissue. The marrow, where present, is fatty or fibrous. There may be small bone cysts filled with reddish gelatinous material. Sometimes small sequestra are to be found in the femur, tibia, and bones of the skull.

The capacity of the skull is not generally diminished. Wyllie found reduction in capacity of the eye sockets in some of the skulls at the Royal College of Surgeons. Prominence of the eyes may be thus explained.

In a case seen by one of us (M. J. C.) at St. George's Hospital, London, under the care of Dr. Collier, deep grooves were formed by the frontal veins on the frontal bone.

Microscopically, according to Butlin, the Haversian systems are diminished in number but enormously widened, and many are confluent. The sides are "eaten out" to form Howship's lacunæ, said to be so characteristic of inflammation of bone. New, incompletely developed bone is evident beneath the periosteum. Fibrous tissue and fibro-cells are abundant. Osteoblasts figure frequently in microscopical

sections. The trabeculae are fairly evenly distributed, and amongst them (as Knaggs points out) there are internal "lines" or darker-stained markings.

There is therefore a double process of rarefaction, or malacia, and new bone formation of connective tissue origin, or proliferative osteitis. This process is known as halisteresis, and Dawson and Struthers, who discuss the pathology of the disease fully, define the process as a progressive decalcification and resorption of the old bones and replacement by an osteoid tissue. Prince says that any of the three following processes may predominate: (a) absorption of the bone, (b) new formation of bone tissue without calcification, (c) new formation of bone tissue with calcification. After histological examination Packard, Steele and Kirkbride came to the conclusion that the processes in their case were: (1) absorption of healthy bone, (2) formation of new bone, but in no way connected with the absorption process, (3) failure of calcification of new bone, (4) destruction of the regular structure of the bone and addition of new uncalcified bony tissue, (5) formation of a giant-celled sarcoma in the skull.

It appears that sarcomatous malignancy is of more frequent occurrence in the disease than carcinomatous growth. In Cone's case the marrow showed myxomatous, and in places fibro-myxomatous, degeneration. The capillaries were varicose, the veins were distorted, and there were areas of hæmorrhage. Some of the vessels were ossified, others thrombosed, fibrosed and incorporated in newly formed bone. Fat was scanty, and here and there were irregular islets of bone in the marrow. A good deal of brown pigment was present in bone cells and stroma. In none of our cases was there any X-ray evidence of malignant changes in the bone.

Whereas ordinary bone requires three to four days for decalcification, in the laboratory, Pickard, Steele and Kirkbride noted that decalcification of the clavicle from their case was complete in twelve hours, thus showing the deficiency in calcium salts.

Changes have been recorded in the spinal cord, and it has been suggested that the changes here are primary and that the bone pathology is due to trophic disturbance. It is more likely, however, that any abnormality in the cord is due to pressure of bony outgrowths from the vertebrae. There is little uniformity in the description of damage to the cord. Thus Stilling described a peri-ependymal sclerosis in his case. In another instance von Recklinghausen remarked on the masses of round cells cuffing the blood-vessels of the cord. Whilst Gilles de la Tourette and others have reported sclerosis of posterior and lateral columns, with extensive degeneration of blood-vessels, Marie and Leri found syringomyelia unexpectedly at necropsy in one case.

The arteries may be so calcified that their X-ray shadows may be as dense as that of bone. This arterial degeneration was well shown in the case recorded by Jones and Holland. Da Costa, Funk, Bergeim and Hawk state that there is more magnesium in the arteries than in the bones.

Piney has examined the blood of five cases. He found no anæmia but there was a basophilia varying between 1·7 per cent. to 4 per cent, and an eosinophilia from 6·8 per cent. to 10 per cent.

Some workers have found a slight increase in the inorganic constituents of the bones and a decrease in the organic. Others have found the opposite to be the case. Da Costa, Funk, Bergeim and Hawk have found marked calcium retention in two cases they investigated.

SYMPTOMS.

The onset is insidious and progress is gradual. Pain in legs, thighs or hip-joints, especially after walking or other exercise, may be first symptom. Pain may be worse at nights as has been noted in the cases recorded by Waterhouse, Pick, Watson, Roth, Manwaring-White and Kilner. Elting suggests pain to be due to distension

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of periosteum. Occasionally cramp in the legs is felt, but usually pain is described by patient as "rheumatic." Muscles may be tender to pressure.

It is only occasionally that the patient notices bowing first. This is usually pointed out by friends, as is also the shortening of the stature. Tubby's patient was astonished when asked how long he had been "bandy-legged." There is clumsiness in moving about, together with lack of bodily and mental energy. Muscular weakness is common. Movements at joints may be restricted. The condition of the individual bones has been noted in the description of the cases.

Often the first complaint is dyspnoea or palpitation; sometimes vertigo or cedema. The skin may be pigmented in places.

Mention may be made of the large number of cases recorded with a systolic murmur at the apex of the heart. In Hurwitz's six cases three had marked apical systolic bruits. Also the number of cases described with associated abdominal herniæ is large. Silcock noted an instance with a strangulated right femoral hernia. The frequent occurrence of malignant disease with osteitis deformans was stressed by Paget. Jenkins has found an associated deafness. He says:—

"I have examined only nine cases of osteitis deformans from the otological standpoint. They all had obvious lesions of the skull bones and they were all suffering from deafness in some degree and I think it may be accepted that deafness is not obvious until the skull bones are affected. . . . The deafness found in all cases of osteitis deformans affecting the head in a marked degree has some characters of typical oto-sclerosis deafness."

The average age of these nine patients was 65 years. Sir J. Dundas-Grant described two cases of osteitis deformans with deafness. Prince mentions two cases of hyperostosis cranii with deafness. One of these subsequently developed Paget's disease.

Generally mental symptoms are absent, but Fritz records an instance where the patient suffered from delusions and had to be sent to an asylum. Fussel described a typical case in a male aged 78 with senile dementia. Southgate recently reported a case of osteitis fibrosa with maniacal symptoms. In this case, which also displayed gangrene of the finger tips, multiple sarcomatous growths were found in the bone on post-mortem examination. Joncheray's patient and one other member of the family were insane.

Remarkable amongst the records is the series noted by Wyllie, who reports two cases with diplopia and deafness due to foraminal compression of the cranial nerves involved, and in two cases also there were signs of constriction of the spinal cord. In both the latter, decompression operations were performed. In one case the cerebro-spinal fluid yielded Froin's syndrome. Blindness also developed in four of Paget's cases.

In our series of sixteen cases, thirteen complained of "rheumatic" pain in the lower limb, and in all of them this was the first symptom. "Cramping" pains in the muscles or behind the knee were experienced in two cases. In three of the cases muscular weakness was an early symptom. Bending of the limb bones or enlargement of the head was not noticed as a rule till later. Three of the patients experienced spontaneous fracture of the femur; in each case there was a preceding history of pain. In one of our cases the patient suffered from choroiditis and retinal hæmorrhages.

X-RAY APPEARANCES.

From the radiological investigation of these sixteen cases, it was found that the order of frequency of affection of the bones was as follows: skull, tibia, femur, pelvis, then, less frequently, radius, hand, foot, humerus and ulna.

The bone changes of Paget's disease will be appreciated most readily by a consideration of the X-ray changes which were found (1) in the skull, (2) in the spine, (3) in the pelvis, (4) in the long bones.

Skull.—It is a striking fact that in all our cases, with only one exception (Case XIII), no matter how localized or extensive the changes in the rest of the skeleton may have been, X-ray changes of greater or less degree were found in the skull.

The earliest change noticed in the skull appears to be a blurring of the outline of its surface, with or without thickening of the calvarium. The skull is now evidently soft, for even in this stage a certain degree of flattening, under the action of gravity, is seen to have taken place, the whole calvarium giving the impression that it has, as it were, been stroked backwards from the forehead.

Progressive thickening of the calvarium now takes place, the changes affecting chiefly the outer table (fig. 1, p. 15). Lime salts are, however, not laid down in a uniform manner in this thickened bone, for we find irregularities of opacity in the bone, first over part of the calvarium, later over the whole of it (fig. 2). This irregularity of calcification results in the appearance of "islands" of dense bone in the part of the skull seen broadside on, and in irregular excrescences and indentations of the part seen tangentially. This would indicate that the new bone that is laid down does not enjoy the more or less systematic calcification which is found, say, in ordinary subperiosteal bone repair, but that the lime salts are either laid down in an irregular manner, or that as soon as they are deposited they are irregularly re-absorbed in places.

As this process of irregular thickening of the outer tables progresses, the differentiation between outer and inner tables becomes lost, and finally the inner table also loses its clarity of definition and shows the same ill-defined ragged appearance as the rest of the bone. In many of the cases the sutures were seen to be obliterated and the vascular channels to be ill defined and broad. In the later stages the thickness of the calvarium has become increased to several times that of the normal; the bone now appears to be made up of numerous ragged patches and tufts of calcified tissue, with more translucent areas between them (fig. 3, p. 18).

It does not follow that the skull of every case will progress to this advanced degree, for it seems likely that at any stage of the disease the condition may become stationary. In one case (Case VI) in which the changes in the skull were very slight, and in which only one other bone (*viz.*, the femur) was affected, this certainly happened, the skull not only returning to its normal structural appearances, but also apparently losing its flattening and recovering its normal shape. Concurrently with the improvement in the condition of the skull, this patient's femur, which had fractured spontaneously, united and showed definite evidence of improvement, the bone finally becoming well organized and the disease becoming stationary. In most of the cases there appears to be no relationship between the degree of change visible in the skull and that found in other parts of the skeleton. The skull may only show slight bone changes, and yet other bones, such as the pelvis or femur, may show advanced changes, or vice versa.

The skull changes described in the vault may be also present in the base (fig. 3, p. 18), though they are not so readily demonstrated by X-rays in the latter situation. It will be obvious how such changes taking place in the base may cause compression of the nerves and vessels passing through the various foramina. In the lateral views of the skull it is interesting to note that in three cases (Cases IX, XII and XIV) the pituitary fossa appeared to be enlarged. Whether this apparent enlargement should be regarded as an indication of a lesion of the pituitary gland is questionable, for the actual size of the pituitary fossa may be normal and only appear to be enlarged because of deficient calcification of the superficial layer of bone forming its walls. That such deficient calcification exists is shown by the appearances in one of our cases (Case XIV) of the posterior clinoid processes, which, to X-rays, are in places translucent.

The appearances of the frontal sinuses varied, some being big, with thin anterior

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walls, others being small with thick anterior walls, and some being ill defined because of defects in calcification of the walls.

(2) *The Spine*.—Primary bone changes of Paget's disease were only shown in the spine in about half of the cases. These changes consisted as a rule of a woolly or blurred appearance of the vertebral bodies, with a tendency to coarse, blurred vertical striæ at the periphery and horizontal striæ near the upper and lower surfaces. Unfortunately in the majority of the cases only antero-posterior views were taken; the spinal deformities would have been better seen in lateral radiographs.

In one of the remaining cases the X-ray appearances of the spine were normal; in two cases the only bone changes shown were those of chronic osteo-arthritis.

In a few of the cases the vertebral bodies appeared to be flatter and broader than normal.

(3) *The Pelvis*.—In fifteen out of the sixteen cases of the series definite and characteristic bone changes were seen in the pelvis. In nine cases there was a deformity of the pelvic cavity, the pelvic brim having become triangular in shape (fig. 4, p. 19). This would indicate that the bone was, or had been, soft, the deformity being produced by the upward and inward thrust of the heads of the femora when supporting the body weight. In most of the cases the iliac crests showed a thickening and a splaying out, the bones thus taking on a massive-looking appearance, evidently belying their real strength. In most of the cases the outline and structure of the pelvis were blurred, the general appearance of the bone suggesting a granular or amorphous body-ground with faint coarse indistinct striæ running through the cortex (fig. 4). In only one case was the granular appearance alone seen, without the striæ or trabeculæ; whilst in two of the cases the trabeculæ were particularly well defined and clear cut.

(4) *Long Bones*.—During the active stage of the disease the long bones show changes in (1) bulk, (2) shape and (3) substance.

(1) *Changes in bulk*.—The change in bulk manifests itself chiefly in an increased thickness of the bone, the cortex often becoming several times its normal thickness.

(2) *Changes in shape*.—Although the thickness of the bone may be markedly increased, the new bone is evidently both soft and brittle. Its softness is indicated by the deformities produced, consisting mainly of a bending which usually takes place in such a manner as to accentuate the normal curve of the bone (fig. 5, p. 20). This bending has been variously attributed to (a) static effects due to the action of gravity, (b) muscular action, (c) an increase in length, as well as in thickness, of the bone, resulting in a bowing owing to the ends being kept at a more or less fixed distance apart by the tonic contraction of the muscles, or by attachment at its ends to an unaffected bone.

(a) The first theory is supported by the deformities shown, for the bones in which the greatest deformity takes place are the bones by which the body weight is supported, namely the tibia and fibula, femur and pelvis (figs. 4, 5, pp. 19, 20).

(b) That gravity is not the only agent at work is, however, indicated by the fact that bowing may take place in such bones as the radius and ulna, where of course gravity could produce no bowing. In further support of this theory is the fact that where deformities of the long bones had taken place the bowing was almost invariably such that the concavity of the bend was directed towards the more powerful groups of muscles in each case, viz., the adductors and flexors of the thigh, the muscles of the calf and the flexors of the forearm. In one case only was this rule not observed, viz., in the case of the radius of one patient which showed an "S"-shaped bend.

(c) That the total length of bones increases is beyond doubt, but that this phenomenon may play a less important part in the production of bending than the action of gravity and muscular contraction is suggested by Case II, in which, on the convex anterior aspect of the tibia, no fewer than twenty incomplete fractures of the

bone are shown (fig. 8, p. 24). These are more likely to have been produced by bending of the softened bone under the action of gravity, with a resultant strain on the convex anterior border and so causing transverse cracks to appear.

(3) Changes in substance.—As previously stated the bones are, in the active stage of the disease, soft and brittle. At the same time as the thickening takes place there appears to be a simultaneous process of irregular decalcification. Or to express it in a different way, the new bone which replaces the old or normal bone is deficient in lime salts. It is presumably during this rarefactive stage that deformities are most likely to take place.

When calcification takes place in the rarefied bone this happens in an irregular and abnormal manner and, it would appear, in two ways: (1) by a more or less generalized deposit of calcium throughout the cortex, producing a granular mortar-like, or amorphous appearance (fig. 8, p. 24); (2) by the formation of coarse irregular striae running mainly in a longitudinal direction (fig. 5), or the direction of the normal lamellae of the particular bone in question, as in the *os calcis*.

Whether these two processes take place simultaneously, whether the amorphous stage precedes the trabecular stage, or whether the trabecular stage can take place without any preceding or accompanying amorphous stage, is not evident. But in any case the end result appears to be a tendency to trabeculation, the trabeculae running more or less longitudinally through the cortex (fig. 5, p. 20). The criss-cross trabeculae, which are seen in the central portion of the long bones, are probably not medullary but are the cortical trabeculae seen "broadside-on" through the more translucent medulla. There is often, however, a lack of differentiation between cortex and medulla, the former encroaching on the latter.

As the disease progresses the trabeculae take on a gradually changing appearance. In the earlier stages the trabeculae are faint, coarse and ill defined (fig. 4, p. 19). As time goes on they become denser and more clearly marked, till finally their outline becomes absolutely clear cut (fig. 7, p. 22). When this has taken place it would appear that the disease, in that particular bone at any rate, has run its course and is becoming quiescent.

It is a remarkable fact that whenever a bone affected by Paget's disease was radiographed after a recent fracture, the bone was always in the stage of amorphous calcification or of early fluffy trabeculation. The tibia in which multiple cracks had occurred (fig. 8, p. 24) was also in the fluffy amorphous stage.

In the case in which radiographs were obtained after union of a fracture the trabeculae had become stronger and more clearly defined, and could, moreover, be readily traced up to, and through, the site of fracture. The formation of these dense, well-defined trabeculae appears to be Nature's method of bringing the disease to a local termination. In no case have we come across a fracture taking place when the bone was in the final well-trabeculated or sclerosed stage. As the changes mentioned take place in the substance of the bone, corresponding changes take place in its outline. At first the outline is rough and ill-defined (figs. 4, 5, 8, pp. 19, 20, 24), but as increasing sclerosis takes place its definition becomes clearer (fig. 9, p. 24).

A further feature which is worthy of consideration is the frequent occurrence of long ovoid, translucent areas in the bone which would suggest the possible formation of cysts. This is strikingly shown in Case IV. When this case was first examined the knee area alone was radiographed. In the upper end of the tibia there was found a large ovoid, translucent area, covered by a thin clearly defined layer of bone, the general appearance presented at that time suggesting "fibrocystic disease" with a large cyst (fig. 6, p. 21). When one of us (R. E. R.) saw the man three years later, in addition to X-raying the tibia (fig. 7, p. 22), skiagrams of the skull, spine, pelvis, and other bones were taken; they showed changes which were typically those of osteitis deformans. The translucent area in the upper end of the tibia was traversed by well defined longitudinal trabeculae.

The occurrence in the cortex of small elongated translucent areas was noted in several cases. One has no proof that these are cystic in nature, but their X-ray appearances would certainly suggest this interpretation; if it be correct, cyst-formation in Paget's disease is by no means an infrequent occurrence. Possibly, on the other hand, they may be merely areas of non-calcified osteoid tissue.

It will be noted that the changes which we have described, especially in the pelvis and long bones, would conform with the changes which are found in the disease called osteitis fibrosa. In fact, had only one of these limb bones been examined in each case it is possible that one might have regarded that particular case as being one of osteitis fibrosa. But when, on radiographing the skull and other bones, one finds bone changes which are identical in nature with those found in cases of obvious and undoubted Paget's disease, there is no alternative but to regard them all as being cases of osteitis deformans.

One might be tempted to call the mono-osteitic variety "osteitis fibrosa," but, from the X-ray point of view at any rate, "generalized osteitis fibrosa" and "osteitis deformans" appear to be one and the same disease.

When investigating these cases one is struck by the apparently haphazard manner in which the bones of any particular patient may be affected. Thus we may get one rib on one side involved and another rib higher up or lower down on the other side; or the metacarpal bone of one finger with the phalanx of another finger (fig. 9, p. 24), and so on. There is no apparent symmetry about the changes in the skeleton; even in the pelvis one side as a rule showed a greater degree of deformity than the other, though in every case both sides of the pelvis were affected.

Apart altogether from the bone changes characteristic of the disease, one is impressed by the frequency of occurrence of associated bone changes of chronic osteo-arthritis. Seven out of the sixteen cases showed X-ray evidence of osteo-arthritis of the knee (fig. 7, p. 22), hip, ankle or spine. Though the majority of the cases were well advanced in years and therefore possibly liable to arthritic lesions, yet the existence of chronic osteo-arthritis in so many of them might possibly indicate that toxic absorption of some sort may play a part in the causation of the disease. On the other hand, the association of chronic osteo-arthritis may be merely a coincidence.

One is also impressed by the frequency with which calcification of arteries is shown in the skiagrams (fig. 6, p. 21). This condition should probably be regarded as a complication rather than a cause of the disease. It is presumably merely a further illustration of the existence of a perverted calcium metabolism, normally controlled by the parathyroid gland, lesions of which have been recorded in cases of Paget's disease where post-mortem examinations have been made.

VARIETIES.

A mono-osteitic form has been described (Schlesinger, cited by Locke). Joncheray has described two varieties: (1) Painful, (2) painless variety. Guaciero, Roth, Laming Evans, Bowlby and Hurwitz reported cases in which only one bone was affected. Paget's disease may be unilateral to start with. Pescarollo and Bertolotti described such a case and pointed out that the temperature on the affected side was 0.5° C. higher than on the other side. Klippel and Weil also reported a case in which lesions were right-sided only.

The lower jaw is seldom hypertrophied. In Bernard Myers' case there was a prominent lower jaw, but the sella turcica was normal. In Manwaring-White's case the lower jaw was enlarged on one side, and in Parry's instance the chin point of the lower maxilla was enlarged, but other bones of the face were regular. Bowlby, Fitz, Lewin, Wyllie and Goodhart recorded cases with unduly enlarged lower jaw. In Jefferson's case the lower jaw was prognathous and the face presented an asymmetry.

COMPLICATIONS.

(a) Fractures are not rare. Spontaneous fractures occurred in three of our cases. A peculiarity of some of these fractures is their incompleteness, and they are found at points of greatest extension. Such partial fractures may be multiple; a good example of these may be noted in the tibia of Case II, when twenty incomplete fractures were found at X-ray examination. Generally when fractures occur they unite well with normal healing (note our Cases I and VI), but exceptionally non-union may be present for many years. One case of Lewin's displayed several fractures which at the end of twenty years were still ununited.

(b) Osteo-arthritis is a frequent association.

(c) The most serious complications arise from the arteriosclerosis and atheroma.

(d) Pulmonary troubles such as bronchitis, emphysema and tuberculosis are not uncommon.

COURSE AND PROGNOSIS.

The disease is chronic, progressive and crippling. As judged from the age of onset and long duration it does not shorten life to any great extent.

Owing to deficient expansion of the chest patients are liable to diseases of the lungs, and the arterio-sclerosis, which is often extreme, is a factor which may give rise to cardiac and associated troubles. Amerson sums up the prognosis thus: "And yet, all things considered, the cases of even marked grades of Paget's disease do enjoy fairly good health."

DIAGNOSIS.

The age of the subject, insidious onset, characteristic deformities, and X-ray appearances of the bones, present a picture fairly easily recognized. The value of radiographic examinations in the diagnosis of osteitis deformans may be illustrated by the fact that of our series of sixteen cases only half showed sufficient clinical evidence before they were X-rayed to indicate Paget's disease. Of the remaining eight cases three were radiographed because of recent fracture, three because of pain in the knee and hip, one because of choroiditis and retinal hæmorrhage, and one for a suspected renal lesion. In each of these cases the local X-ray appearances suggested osteitis deformans, the diagnosis being subsequently confirmed by a fuller radiographic investigation of the other bones of the body, changes being then found in parts where clinically there was nothing to suggest that any abnormality or disease existed. Fitz lays stress on the multiplicity of the bones affected as a constant characteristic.

The condition may be differentiated from leontiasis ossea, osteomalacia, acromegaly, osteoporosis, rickets, syphilitic hyperostosis of tibia, secondary pulmonary hypertrophic osteo-arthropathy. It is, of course, conceivable that on rare occasions any one of these conditions may be associated with osteitis deformans.

TREATMENT.

In the present state of our knowledge treatment is empirical. Opiates, salicylates and bromides may be tried for relief of pain. Tonics, rest and massage may be useful. Peckham suggests the cautery to painful points. Munford noted improvement in one case "on lines which would be used for rickets." The patient was sent to the country, and enjoyed fresh air and sunshine, and was given cod-liver oil.

Byrom Bramwell noted improvement in a case by the exhibition of adrenalin chloride. Myers relieved pain with sodium salicylate and Manwaring-White relieved it by giving thyroid. In three of our own cases (I, II, III) parathyroid, thymus, calcium lactate and potassium iodide were used without avail. The most striking case of our series from the therapeutic point of view is Case VI. This patient, under the care of Dr. Basil Murphy, of Wallasey, showed undoubted radiological evidence of improvement in the only bones affected (*viz.*, the femur and the skull) during the period of observation. The therapeutic agents utilized in this case were the following:

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mistura alba, cod-liver oil, calcium lactate, thyroid, parathyroid, thyroprotein, and "milk in abundance," with, of course, efficient splinting.

Tubby saw improvement with bone-marrow and thymus, also with cod-liver oil and calcium lactate and on a diet rich in proteins but sparing in carbohydrates, but no effect from treatment with phosphorus.

Lewin suggests a phosphorus pill, gr. $\frac{1}{100}$, three times daily over long periods to be of some use.

Surgery has been tried in a few instances. Roth performed a cuneiform osteotomy on the right tibia of a female presenting features of osteitis deformans in that limb. Afterwards she was fitted with a Thomas's caliper. Union took place in ten months, and after that she was able to walk about without the splint.

Guaciero has performed amputation. Here the tibia alone was involved, and the leg was sacrificed in the hope of arresting the disease. We have not found mention of what happened subsequently.

Knaggs, in his Hunterian lecture, stated that in a case of his Littlewood amputated the affected leg, this being the only obviously diseased member.

The multiplicity of the remedies used, many being but blunderbuss shots at the patient in the hope of doing some good, reflects more than anything else on the lack of knowledge as to the actual causal agents at work.

It is claimed by some (Knaggs, Jefferson) that osteomalacia and osteitis deformans are virtually the same disease, but at different stages. It is possible that sterilization, found useful in some cases of osteomalacia, might similarly cure or stop the progress of Paget's disease. Elliott and Nadler castrated a man of 34 suffering from osteomalacia, but found no improvement after the lapse of six years. Possibly the less drastic Steinach operation will in future be given a trial in this disease.

SUMMARY AND CONCLUSIONS.

- (1) We record 16 cases of osteitis deformans.
- (2) Eleven patients were male, 5 female.
- (3) The *etiology* of the disease is doubtful. Possible factors are (i) Toxins, (ii) Endocrine disturbances, (iii) Heredity (or environment), (iv) Syphilis.
- Two of the patients were sisters; 2 of the patients showed a positive Wassermann reaction.
- (4) All the patients, except one, were above the age of 40 years when first seen; in only 2 cases had symptoms appeared before the age of 40.
- (5) In 11 cases the *earliest* symptom was pain (of a "rheumatic" nature) in the lower limbs. Muscular weakness, cramps, deformities, fractures and head enlargement were usually later manifestations.
- (6) In 3 cases spontaneous fracture of the femur occurred; in 1 case twenty incomplete "cracks" were found, radiologically, in the convex anterior border of the tibia, and 3 in the femur.
- (7) *Pathology*.—The process is one of "halisteresis," or "a progressive decalcification and resorption of the old bone and replacement by an osteoid tissue" (Dawson and Struthers).
- (8) The *X-ray appearances* illustrate the various stages of this pathological process. In the skull the earliest X-ray change is a blurring of the outline of the calvarium, with, as a rule, thickening and "flattening"; the later changes are those produced by progressive thickening with irregular calcification in the osteoid tissue, frequently affecting the base as well as the vertex. Enlargement of the pituitary fossa was shown in 3 cases.
- In the long bones, one of the features is the production of "trabeculae" in the thickened cortex. These are at first faint, coarse, and ill defined, but later become denser and more sharply defined. The stage of the disease in any bone can be gauged by the type of trabeculae shown in the skiagram.

Fractures only occurred when the bone was in the early amorphous or faint, blurred, trabecular stage.

Occasionally, as in the metacarpals, the X-ray appearances indicate a dense granular deposit of calcium in the thickened cortex; in the os calcis, the appearances may be merely those of coarse trabeculae, along the normal lines of lamellation.

(9) In 8 cases the diagnosis of the disease was primarily radiological. Characteristic X-ray changes were found in the skull in 15 cases, pelvis 15 cases, femur 15 cases, and tibia 15 cases. X-ray changes were often found in parts quite unsuspected of disease of any sort. The necessity is thus seen for (i) a local X-ray examination of cases of obscure limb pain, (ii) a general X-ray examination of the skeleton (especially skull and pelvis) in all cases where suggestive local bone changes have been found.

(10) Where local X-ray changes suggestive of "osteitis fibrosa" were found, a general X-ray examination invariably showed appearances which were characteristically those of "osteitis deformans." Radiologically, it is impossible to differentiate between "generalized osteitis fibrosa" and "osteitis deformans."

"Osteitis fibrosa cystica," which may be localized to a single bone, is probably a different disease, or at any rate a different type.

(11) The treatment of osteitis deformans is at present very unsatisfactory.

One of our patients showed definite radiological evidence of improvement on the following treatment: Mistura alba, milk, cod-liver oil, calcium lactate, thyroid extract, parathyroid extract, and thyroprotein. One has no means of surmising which of these was the curative agent; probably each played its own part.

ACKNOWLEDGMENTS.

We wish to express our thanks to Mr. Thurstan Holland and Dr. J. H. Mather for much valuable help, and to the physicians and surgeons of the Royal Infirmary, Liverpool, and of the Victoria Central Hospital, Wallasey, for granting facilities in the investigation of their cases.

REFERENCES.

- ASKANAZY, cited by HARBITZ, *vide infra*. BOWLBY, "Surgical Pathology and Anatomy," 1905. BRAMWELL, *Lancet*, 1908, ii, p. 159. BUTLIN, *Lancet*, 1885, i, p. 519. CARMAN and CARRICK, *Journ. Bone and Joint Surg.*, 1922, xx, p. 45. CHAUFFARD, cited by FITZ, *vide infra*. CORSON-WHITE, *Arch. Intern. Med.*, 1922, xxx, pp. 790-6. CUTLER, *Boston Med. and Surg. Journ.*, 1916, x, p. 175. CZERNY, *Wien. med. Wochenschr.*, 1873, xxiii, p. 896. DA COSTA, FUNK, BERGEIM and HAWK, *Proc. Amer. Soc. Biol. Chem.*, 1914, xvii, p. 30. DAWSON and STRUTHERS, *Edin. Med. Journ.*, October, 1923. DUNDAS-GRANT, *Proc. Roy. Soc. Med.*, 1922-3, xvi (Sect. Otol.), p. 27. ELTING, *Bull. Johns Hopkins Hosp.*, 1901, xii, pp. 343-9. EMERSON, Osler and McCrae's "System," 1909, vi, "Osteitis Deformans," pp. 715-24. ERDHEIM, cited by DAWSON and STRUTHERS, *vide supra*. EVANS, *Brit. Med. Journ.*, 1911, i, p. 1000. FITZ, *Trans. Assoc. Amer. Phys.*, 1902, xvii, pp. 398-405. FRENCH, *Brit. Med. Journ.*, 1903, ii, p. 1152. FUSSEL, *Trans. Assoc. Amer. Phys.*, 1902, xvii, pp. 406-8. GOLDMAN, cited by CORSON-WHITE, *vide supra*. GOODHART, *Lancet*, 1885, i, p. 519. GUACIERO, *Brit. Med. Journ.*, 1908, i (Epitome), p. 61. HARBITZ, *Journ. Med. Res.*, 1915, xxxii, pp. 361-75. HIGBEE and ELLIS, *Journ. Med. Res.*, 1911, xxiv, p. 43. HURWITZ, *Bull. Johns Hopkins Hosp.*, 1913, xxiv, pp. 263-74; *Amer. Journ. Med. Sci.*, June, 1914. HUTCHINSON, *Illus. Med. News*, 1889, ii, p. 169. JEFFERSON, *Brit. Journ. Surg.*, 1915-16, iii, pp. 219-33. JENKINS, *Proc. Roy. Soc. Med.*, 1922-3, xvi (Sect. Otol.), pp. 21-9. JONCHERAY, Thèse de Paris, 1893. JOST, cited by CORSON-WHITE, *vide supra*. KILNER, *Lancet*, 1904, i, pp. 221-3. KLIPPEL and WEIL, *Lancet*, 1909, ii, p. 1452. KNAGGS, *Brit. Journ. Surg.*, 1925, xiii, p. 50. LOCKE, "Oxford Medicine," 1921, iv, "Osteitis Deformans." LUNN, *St. Thomas's Hosp. Reports*, 1883, xiii, p. 43. MANWARING-WHITE, *Brit. Med. Journ.*, 1909, ii, pp. 12-15. MUNFORD, *Clifton Med. Bull.*, 1923, ix, pp. 20-37. MYERS, *Lancet*, 1914, ii, p. 176. PAGET, *Med. Chir. Trans.*, 1877, lx, 37-64; 1882, lxxv, 225-36. PARRY, *Brit. Med. Journ.*, 1912, i, pp. 879-80. PECKHAM, *Amer. Journ. Orthop. Surg.*, 1903, i, p. 130. PESCAROLO and BERTOLOTTI, *Lancet*, 1909, ii, p. 1452. PICK, *Lancet*, 1883, ii, pp. 1125-6. PRINCE, *Trans. Assoc. Amer. Phys.*, 1902, xvii, pp. 382-97. VON RECKLINGHAUSEN, "Die fibröse o. deformierende Ostitis," Berlin, 1891. ROSSWEG, cited by CORSON-WHITE, *vide supra*. ROTH, *Lancet*, 1912, ii, p. 1510; *Proc. Roy. Soc. Med.*, 1922-3, xvi (Sect. Orthop.), p. 49. SCHLESINGER, cited by LOCKE, *vide supra*. SILCOCK, *Trans. Path. Soc. Lond.*, 1885, xxxvii, pp. 383-7. SMITH, *Trans. Med. Soc. Lond.*, 1905, xxvii, p. 224. STAHL, *Amer. Journ. Med. Sci.*, 1912, cxliii, p. 527. STEGMANN, *Wien. klin. Wochenschr.*, 1905, xviii, p. 619. STILLING, *Virchow's Arch.*, 1890, cxix, p. 542. TUBBY, "Deformities, including Disease of Bones and Joints," London, 1912, ii, pp. 561-9. WATERHOUSE, *Lancet*, 1907, i, pp. 1215-17. WATSON, *Bull. Johns Hopkins Hosp.*, 1898, ix, pp. 133-6. WILKS, *Lancet*, 1909, ii, p. 1627; *Trans. Path. Soc. Lond.*, 1869, xx, p. 273. WOLLENBERG, cited by LOCKE, *vide supra*.

Discussion.—Dr. W. H. COLDWELL said that he had collected a few notes on a series of twenty-six cases of Paget's disease, using the term in the broad category mentioned earlier in the evening. The figures compared very closely with those of Dr. Roberts, in that 50 per cent.

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were found accidentally while an examination was being made for some other condition ; the sexes were distributed in the proportion of 60 per cent. male and 40 per cent. female. In his series of cases, pain had not been a noticeable feature ; only eight patients had complained of pain, and in four of these malignant changes were present. The distribution agreed very closely with that described by Dr. Roberts. The most striking feature he had noticed however—one which Dr. Roberts had not mentioned—was the percentage of cases that had shown, or had developed, malignant changes. In no less than five out of twenty-six cases (nearly 20 per cent.) had this occurred. In two of these cases the changes were in the pelvis, in one in the neck of the femur, in one in the shaft of femur, and in another in the humerus. In the case in which the neck of the femur was involved, the lesion was discovered following a spontaneous fracture of the neck. In two cases the pathological report was endothelioma, in another sarcoma, and in the other two no operation was performed before the death of the patient, and a post-mortem examination was unobtainable. He said he would be interested to hear the experience of the other Members present with regard to the question of the supervision of malignancy in cases of Paget's disease.

Mr. THURSTAN HOLLAND drew attention to the fact that in the pre-Potter-Bucky diaphragm days as a rule only small areas were examined, these areas being usually the sites of pain. At this time considerable confusion existed and many cases were described as "osteitis fibrosa" which were undoubtedly, in view of later knowledge, cases of Paget's disease (these being considered to be different diseases). In both books and papers, radiographs of tibiae were reproduced and described under one or other of the above headings, when a comparison showed that they were undoubtedly the same disease. The differences in appearance varied (1) in proportion to the stage of the disease ; (2) according as the destructive or reparative process was in the ascendant. About three years ago he had come to the conclusion that, at any rate from the radiographic point of view, there was no difference between generalized osteitis fibrosa and Paget's disease ; the work of the authors, he considered, fully confirmed this view. It was of the utmost importance to examine all the bones in a suspicious case and not be content with a radiograph of the painful area only—most of the early cases would be sent to the radiologist for the examination of a specific area on account of pain. If the bone changes found gave rise to suspicion, a complete examination would clear up the diagnosis, and for this purpose the bones of the skull and the os calcis were especially important. Changes in the skull were almost always present in Paget's disease, and if present appeared to be pathognomonic. In the os calcis probably the earliest bone changes could be seen. In typical cases of Paget's disease the radiograph of the os calcis—which was apparently unaffected—showed quite distinctly a loss of definition and sharpness in the linear striations. It was of interest to note that in cases of obscure bone conditions, apparently associated with the growth of bone, in young adolescents, the os calcis sometimes showed exactly the same X-ray appearances. In conclusion he (Mr. Thurstan Holland) again expressed his opinion that Paget's disease and generalized osteitis fibrosa were one and the same disease, and that the best name for this condition would be "osteitis fibrosa."

Dr. A. C. JORDAN said he would like to hear more of the clinical side of the disease. Recently, he had seen a case of Paget's disease, sent, not on account of bone disease, but for digestive troubles. Incidentally a swelling on the femur was mentioned. He had found pronounced Paget's disease of both femora, both tibiae, the pelvis and the humeri. The patient admitted having had to buy larger hats the last two years, and, on examination, the skull showed quite evident changes, and the pituitary fossa was larger than normal. This coincided with some of the observations made by the authors and suggested that an endocrine upset was probably responsible for the chief manifestations of the disease. A clinical feature—prominently displayed in the above-mentioned case and said to be present in a fair proportion of cases—consisted in a somewhat unrestrained attraction for persons of the opposite sex. The text-books did not mention this, but this feature no doubt supplied further evidence of disturbance of the endocrine balance.

Dr. SHILLINGTON SCALES called attention to the fact that several cases of malignancy supervening upon Paget's disease had been reported, and suggested that it would be well to consider this as a possibility. It was unfortunate that we had so few records of the end-history of cases of Paget's disease, which by the help of X-rays had been shown to be of quite frequent occurrence.

Dr. F. PARKES WEBER remarked that an additional argument in favour of the pathological identity of Paget's osteitis deformans and Recklinghausen's generalized type of osteitis fibrosa was that disease of the parathyroid glands had been also found present in the latter (A. Gödel).

Section of Electro-Therapeutics.

President—Dr. ALASTAIR MACGREGOR.

The X-ray Diagnosis of Animal Parasites (Helminthes) in Man.

By J. F. BRAILSFORD, M.B. (Birmingham).

THE possibility of X-ray diagnosis depends on the calcification of the parasites or their location in the body.

Most of the encysted embryos undergo calcification; this may follow as the sequel to the death of the parasite, or as some authorities believe it to be, a protective reaction of the tissues of the host with the subsequent death and calcification of the parasite, living embryos having been found in cysts, the outer walls of which showed calcification. Leuckart says that incipient calcification can be detected in *Trichina* in six months, but that it takes fifteen to sixteen months for complete impregnation of the parasite with lime salts. X-rays are therefore not of much value in the early days of infestation unless the parasite is situated in the lung-fields.

The presence of the calcified parasites does not exclude the presence of the living parasites. One has seen echinococcal cysts calcified to the hardness of stone, existing in the liver with cysts containing living scolices. This may be due to a further more recent infestation. Calcification may occur primarily in the parasite itself, in the cyst-wall, or in the reactive sheath of the host's tissues.

When the parasite is located in the lung as in echinococcal cysts, their relative density permits of an early diagnosis.

In bone, where active absorption takes place with the development of the parasite, the radiograph will detect changes in the early stages, but the diagnosis will not be easy.

The chief parasitic conditions detected by X-rays are echinococcal cysts and the cysts of *Cysticercus cellulosæ*, but the X-ray appearance of conditions such as calcified *Trichina*, *Paragonimus westermanii*, onchocerci, *Ascaris lumbricoides* and *Bilharzia* have been described.

Hydatid Cysts.—This term is usually applied to the cysts of *Tania echinococcus*, which are much the commonest of the parasitic cysts occurring in man in this country. There is no tissue in the body in which these cysts have not been found, and the appearance of abnormal shadows of rounded or irregular structure with evidence of partial or complete calcification, should lead one to consider hydatid cysts in the differential diagnosis.

There are two species of this parasite. In one, the commonest, the cysts are single. In the other, the cysts form a honeycomb structure, separated from one another by fibrous walls—the so-called *Echinococcus multilocularis*.

Taking the averages of many workers, the distribution of echinococcal cysts is as follows:—

Liver, 65 per cent.; lungs, 10 per cent.; kidneys, 7 per cent.; other abdominal organs, 8 per cent.; cranial cavity, 7 per cent.; bones, 2 per cent.; other organs, 1 per cent.

In all these sites they may be detected in the radiograph if the cysts have undergone calcification. The density of the shadows cast depends upon the stage of calcification. When completely calcified the shadows are denser than those cast by bone. They may be spherical or very irregular in outline: the spherical calcified cyst-walls frequently contain daughter-cysts and scolices. In one of the cases on which I saw the post-mortem made, the patient had a large calcified hydatid cyst situated against the posterior wall of the bladder through which daughter-cysts had escaped into the bladder and been detected in the urine. The calcified cyst-wall in this case was $\frac{1}{4}$ in thick.

But it is usually the cysts which are located in the lung-field which are diagnosed

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by X-ray (fig. 1). These are often found as a result of a radioscopic examination of a patient who has had an hæmoptysis and tuberculosis is suspected; but they may be detected quite accidentally while screening a patient who has given no sign of pulmonary disease. In the latter case, the cysts, the contained fluid being under pressure, appear as isolated spherical shadows of uniform density with sharp, regular borders, varying in size from that of a pea to that of a large orange surrounded by normal lung-tissue. With such a picture there is no other pathological condition for which they could be mistaken. If situated in the mid-line or against the walls of the thorax the X-ray diagnosis cannot be so certain. In the cases of cysts which have caused symptoms the X-ray diagnosis may be certain if the symptoms are caused by

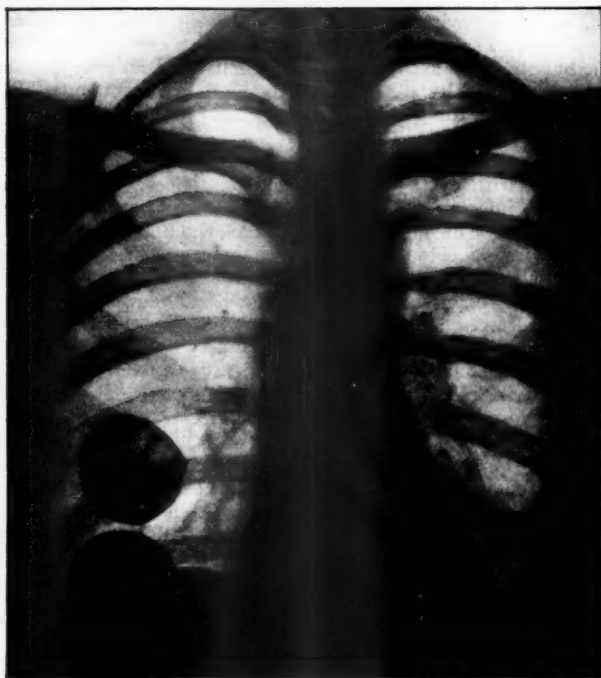


FIG. 1.—Hydatid cysts of lung.

pressure from a large free cyst or if other isolated cysts are present, but the diagnosis may be obscured by reactive changes in the tissues around, or by collapse of the involved lung owing to pressure on the bronchus.

If the cyst is pressing against a bone the latter may be completely absorbed and spontaneous fractures may occur. This has been seen in cysts located in the thorax where the ribs and spinal column and vertebræ have been destroyed. Wherever the cyst is located it tends to assume, owing to its internal pressure, a spherical appearance—a feature which should help one to distinguish it from localized abscesses or fluid collections. The patient may have coughed up daughter cysts, or scolices, or expectoration which was bile stained owing to the bursting of a cyst into a bronchus.

All the radiographic evidence may be a raising of the affected side of the diaphragm.

usually the right, with, perhaps, fixation by adhesions. In those cases in which clinical evidence suggests a ruptured cyst of the liver emptied by way of the bronchus the injection of lipiodol may be of service. In doubtful cases the diagnosis must rest upon the finding of scolices, differential blood-count, complement fixation, &c.

The artificial puncture of the cyst may cause serious symptoms from anaphylaxis, urticaria or secondary infestation, but it has been used with success for the destruction of the cyst. Where the cysts are located in the liver one may see a raising of one side of the diaphragm, or a local spherical protuberance may be seen through the right lung base. Cysts in the liver and other abdominal organs may be demonstrated by the pneumo-peritoneal method.

In the bone the cysts present the appearance on the radiographs not unlike that

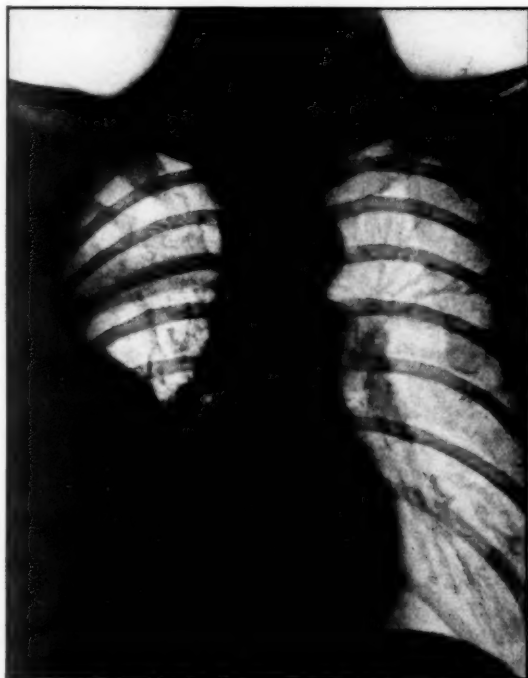


FIG. 2.—Hydatid cysts of lung and liver (infection from tame fox).

of a myeloid sarcoma, as can be seen from the illustrations in Bauer's article on "Echinococcus of the Tibia." The first evidence of this pressure may be a spontaneous fracture of the bone invaded. I have not met with any human bone cyst which, on examination, has proved to be echinococcal. As regards the frequency in bone, Gangolphe found 52 cases with cysts in the bones in 3,000 cases, while Alexinsky found 37 cases with cysts in the bones in 1,950 cases; in 75.21 per cent. of his cases there were cysts in the abdomen.

This parasite is much more common in this country than is usually supposed. While investigating pathological conditions in food animals for a period of years before the war one saw organs of sheep, cattle, and pigs infested with it every day. In

cattle it was no unusual sight to see livers which weighed over 200 lb. due to extensive infestation with hydatid cysts, the normal weight being about 16 lb. The lungs of sheep may be so involved that the cysts appear to be separated by very little normal tissue.

In 1921 I investigated 11 cases in man which occurred in Birmingham. In six of these cases the cysts were in the liver; in one, the cyst, as already described, was against the bladder; in another, the kidney was almost destroyed by a large collection of cysts, some partly calcified; in another there was a calcified cyst of the spleen and the omentum; in another there was a cyst of the lung, while in the remaining case the cyst was located in the buttock. In all these cases a definite history was obtained of very close association with a pet dog, but I was unable to examine any of the dogs for the presence of the adult worm.

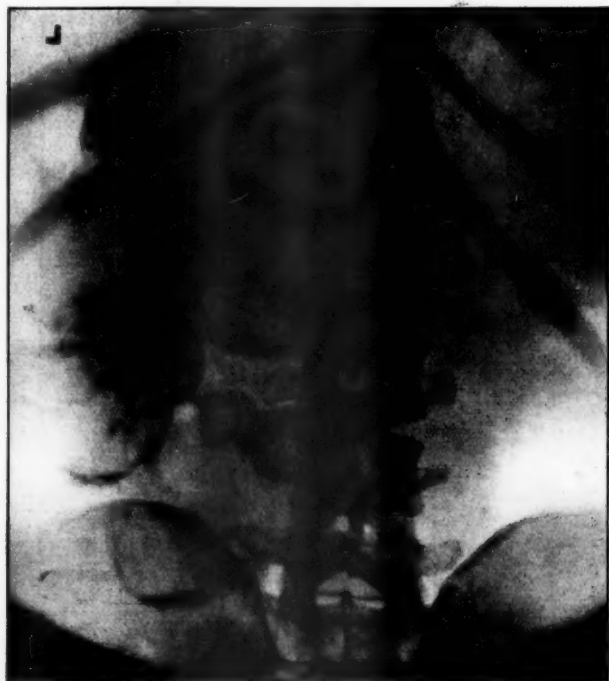


FIG. 3.—Old pyelonephrosis resembling calcified hydatid cysts.

On pointing out the frequency of the disease to Sir John Robertson, Medical Officer of Health for Birmingham, it was arranged that I should make post-mortem examinations on 100 dogs to see what percentage of town dogs harboured the parasite. The alimentary canal of each dog was opened throughout its whole length, but in no case was *Tænia echinococcus* found, though 65 of them were harbouring other species of tapeworm.

The only three specimens of intestine bearing *Tænia echinococcus* which I have seen have been taken from foxes, and in a patient whom I recently X-rayed for echinococcal cysts of the lungs and liver there was a history of the patient keeping in the house a fox which she had trained to take chocolate from her mouth (fig. 2).

These facts lead me to think that the fox plays a greater part than is usually supposed in the dissemination of this parasite, particularly among food animals. The fox is probably infected by eating slaughter-house refuse which is sometimes spread over fields for manure, or by eating infested lambs.

Radiographically, the differential diagnosis of hydatid cysts is as follows:—(a) *In the Thorax*: (1) Aneurysm of the heart, aorta, or its main branches; (2) Sarcomata and secondary tumours; (3) Mediastinal glandular enlargements; (4) Localized empyemata or abscesses; (5) Caries of the spine with abscesses; (6) Dermoid cysts. (b) *In the Abdomen*: (1) Calcified glands; (2) Calcified tumours; (3) Calcified inflammatory lesions; (4) Calculi; (5) Dermoid cysts. (c) *In the Bone*: (1) Bone cysts; (2) Myeloid sarcomata.



FIG. 4.—Old pyelonephrosis resembling calcified hydatid cysts. Lateral radiograph.

Cysticercus cellulosæ.—This parasite has been known for centuries. It is mentioned by Aristophanes in his comedy "The Knights." Its life history was demonstrated by Küchenmeister in 1835, and later by Humbert, Leuckart, Hollenbach and Holler.

The following facts about the development, distribution, and life-history of the parasite may be of help in the radiographic interpretation.

The adult parasite, *Tænia solium*, lives in the intestines of man. It is a rare parasite in this country; the common tapeworm being *Tænia saginata*. The ripe proglottides of the parasite, containing 30,000 ova in each, are passed with the fæces. The ova are liberated during the contractions of the segments, or later by decomposition. If they obtain access to water supply or vegetables the man or animal

(chiefly the pig) eating them liberates the small, six-spined embryos which obtain access to the blood-stream and are carried to all tissues of the body. Here the parasite develops into *Cysticercus cellulosæ*, which appears as a small white body about the size of a millet seed in which the head is invaginated.

The time and process of development were investigated by Gerlach, who gives the following facts: (1) Cysticerci twenty days old; a delicate transparent vesicle of the size of a pin's head without an enveloping membrane; (2) Cysticerci forty days old; enveloping membrane still very delicate: of the size of a mustard seed or sometimes larger; head very plain; sucking discs and a circle of hooklets, recognizable but not completely developed.

(3) Cysticerci sixty days old; enveloping membrane of the size of a pea; head projecting somewhat from the vesicle as a faint white button-like structure. Hooklets and sucking discs completely developed; some difference in size. (4) Cysticerci 110 days old: all about the same size, head free from the enveloping membrane which lies invaginated into its caudal cyst. After the head is forced out the cysticerci have the form of a flask.

These cysticerci are said to occur not only in man, but in the pig, dog, rat, cat and apes.

Man is infested with the adult parasite when he eats *Cysticercus cellulosæ* in "measly pork" imperfectly cooked. The rarity of the adult parasite in this country is probably due to the custom of well cooking pork and the greater difficulty of the parasite in development, while the frequency of *Tænia saginata* is due to the under-cooking of veal or beef which is not usually so extensively infested as pork. It is strange that whereas one saw about four cases of *Cysticercus cellulosæ* in pork in a year and no cases of *Cysticercus bovis*, all tape-worms which have been sent to me for identification have been *Tænia saginata*.

Radiographically, *Cysticercus cellulosæ* has been described in human muscles by Sick, Geipel, Fischer, Stieder, Pursche, Pichler, Köhler, and Saupe.

In some of these reported cases cysts were first found at post-mortems and X-ray examinations were then made of portions of muscle as in the case reported by Geipel. In others, the diagnosis of *Cysticercus cellulosæ* was accidentally made while examining radiographs of fractures. In one or two cases the patient was X-rayed to determine the nature of small hard nodules to be felt under the skin. In the case reported by Köhler, the patient was suffering with sciatica and rheumatic-like pains, and was radiographed to see if any cause could be found. The radiograph showed small, oval homogeneous shadows, 7 to 12 mm. long and 2 to 4 mm. broad, ten to twelve in number, in the soft parts of the knee and calf, two or three in the loins, which appeared to lie in the direction of the muscle fibres. An excised cyst was found, microscopically, to be *Cysticercus cellulosæ*.

Geipel counted 198 shadows in the thigh in his case at post-mortem; these varied in size from that of a pin's head to 2 cm. in diameter. No microscopic report was given.

I have had two cases. The first occurred in a pensioner with a fracture of the humerus. The radiograph showed in addition about six shadows which I considered to be *Cysticercus cellulosæ*, but I was unable to get further pictures in confirmation of this.

The second patient, an old soldier, complained of rheumatic-like pains in his hips and legs; he had been previously radiographed and nothing abnormal reported. On first looking at the radiograph of his hip-joint, it gave me the impression that some splashes of water had been made on the film when it was drying, and, but for my interest in animal parasites, I am afraid I should have left it at that. On closer examination I was convinced that the shadows were of calcified cysticerci, and in order to determine the distribution of the parasite I took radiographs of his whole body. These radiographs I have brought for your inspection to-night.

The cysts are shown as oval bodies of about the same size, 4 mm. broad by

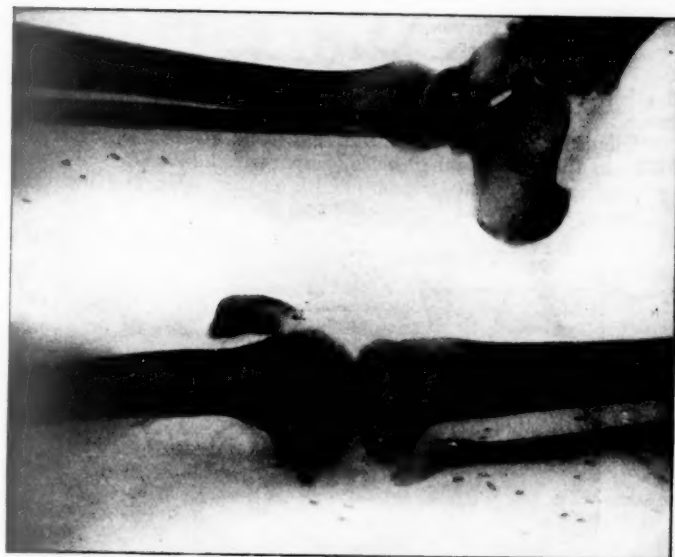


FIG. 6.—*Cysticercus cellulose* in leg



FIG. 5.—*Cysticercus cellulose* in buttocks and thighs.

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8 mm. long, lying in the direction of the muscle fibres. Their distribution (figs. 5, 6, 7) is as follows:—

Thigh, 90; calves, 66; pelvis, 56; thorax, 20; neck 10; loin, 7; upper arm, 8; forearm, 5; hand, 2; head, 2; face, 3.

No cysts are to be seen in the brain of this patient. This may be due to the lack of calcification. Cysts in the brain are usually spherical and larger than those in the muscle.

This distribution is quite different from that seen in the pig, in which animal cysts occur chiefly in the abdominal muscles, diaphragm, lumbar muscles, tongue, heart, muscles of mastication, cervical muscles and brain, but seldom in the viscera. In 400 "measly" pigs examined by Prettner only two showed cysticerci in the eye.



FIG. 7.—*Cysticercus cellulosæ* in thorax.

In man, among eighty-seven cases, Dressel found cysticerci in the brain in seventy-two and in only thirteen cases in the muscles. Von Graefe found cysticerci in the eye in ninety out of 80,000 patients examined for eye disease.

Vosgien gives the following distribution observed in 807 cases of *Cysticercus cellulosæ*:—

Eye and annexes, 370, 46 per cent.; nervous system, 330, 40·99 per cent.; skin and cellular tissues, 51, 6·32 per cent.; muscles, 28, 3·47 per cent.; other organs, 26, 3·22 per cent.

The patient whose radiographs I have shown you said that he had never had a tapeworm. He went through the South African War, and I think it very possible that he picked up his infection there, for, owing to the plague of flies which swarmed in the larders, orders were given for lime to be scattered over the faeces in the

latrines. Later, the food in the larders became so scattered with lime from the flies' legs as to be uneatable. Further, water trenches in the dry season were used as latrines; these would supply the parasite with the most favourable conditions for completing its life history. Nicol has proved that flies can carry the ova of parasites on their legs. Of the other cases diagnosed radiographically, in only one was there a history of tapeworm. In 248 cases of *Cysticercus cellulosæ* examined by Volovatz only twenty-seven had *tænia* in the intestine.

DIFFERENTIAL DIAGNOSIS.

The most likely way in which the presence of *Cysticercus cellulosæ* may be missed is in attributing the shadows on the radiographs of the parasites to defects in the film caused by spots of water being splashed on the drying films. In fact the dried spots of water often seen on films resemble the shape and size of cysticerci.

This error is not likely to be committed if the cysts are very numerous, as in the films of the thigh and leg, but I am sure it is easily possible in the case of a radiograph of the pelvis in which only a few cysts are present.

In the food animals, pig, sheep (fig. 8), and cattle, calcified bodies are frequently seen. These are the calcified sarcocysts produced by the protozoa, *Sarcosporidia*. The radiographic picture of this condition is very similar to that of calcified cysticerci, varying from the microscopic size to that of a haricot bean.

These large sarcocysts have not been recorded in man so far as I am aware, but the illustrations in Geipel's paper on *Cysticercus cellulosæ* are almost identical with a radiograph I have made of a piece of pork (fig. 9) containing sarcocysts, and quite different from the appearance of the radiographs which I have shown and those illustrating the articles of Saupe, Sick, Stieder and the descriptions given by Köhler and Pichler; these bodies were proved microscopically to be calcified cysticerci. Further, Geipel does not state that the bodies shown in his radiographs were proved microscopically to be cysticerci. I have seen many cases of "measly" pork, but the cysts have always been about the same size; as we learn from Gerlach's observations on the growth of the cysticerci, it is only in the early period of development that the cysticerci differ in size; the mature cysticerci he found to be all about the same size. To get the appearance described by Geipel, i.e., "the shadows vary from the size of a pin's head to 2 cm.," one must either consider calcification of the parasites in the various stages of development or partial and irregular calcification of cysts, or assume that his case was one of *Sarcosporidia*.

Saupe mentions the following for consideration with respect to differential diagnosis:—

(1) *Cysticercus bovis*.—A parasite which has only been rarely reported in man in spite of the fact that the adult is the commonest tapeworm in man. Pichler has shown that even these may be hookless *Cysticercus cellulosæ*. (2) *Trichina spiralis*.—These parasites are altogether too small to be mistaken for cysticerci; they rarely exceed 1 mm., and are usually much smaller and occur in greater numbers. (3) *Phlebotomus*, *Small Osteomas*, *Skin Tumours*, *Injected Medicaments*, and *Metal Fragments*, and *Faults*.—These can be excluded by taking a series of radiographs of the other parts of the body.

Trichina spiralis.—The first physician to investigate calcified trichina in human muscle was Hilton, who reported his findings in 1832. In 1828 Peacock gave a specimen of calcified trichina in muscle to Guy's Hospital. He did not discover the worm in its capsule. This was done in 1835 by Paget and Owen, who found the worms in the musculature of an Italian who had died of tuberculosis.

The disease trichinosis was first investigated by Zenker, who found at post-mortem the worms in the intestine of a girl, aged 19, who had been treated in the Dresden City Hospital as a case of typhoid. Virchow and Leuckart investigated the life history of the parasite by feeding some of the musculature to animals. This



FIG. 8.—Sarcosporidia in sheep.



FIG. 9.—Radiograph of Sarcosporidia in pork.

work was confirmed in the outbreaks of trichinosis at Hettstadt (1863), and Hedersleben, in which 500 cases occurred with 129 deaths. The disease is thought to have been brought to Europe by rats from China, where the pigs were often infested.

Calcified trichinae have been found in pigs 9 to 12 months old, and can be seen in the muscle with the naked eye; usually it is only the capsule which is calcified. Leuckart considers that it takes ten years or more before the parasite itself is calcified. Langerhans demonstrated that the worms may be alive after thirty years.

The commonest sites for these parasites are the muscles of the diaphragm, larynx, tongue, and thorax.

Radiographically, these parasites have been chiefly demonstrated in portions of muscle removed at post-mortem, but Levy-Dorn (1923) reported a case of trichinosis in which the worms were discovered in a section of an ulcer of the tongue; he was able to obtain radiographs of the musculature which had the appearance of being dusted with meal. The individual cysts vary from 0.1 to 1 mm. He recommends the systematic radiography of the upper arm for its detection. In view of the preference of the parasite for the muscles of mastication and their occurrence in great numbers, which would tend to obscure the parasite in a thick part, I suggest that it would be preferable to take a radiograph on a dental film of part of the masseter.

I have recently tried to demonstrate the presence of trichina in a portion of the biceps of a man who died from trichinosis, but though, microscopically, the worm can be seen in great numbers, there was no trace of them on the radiograph, no calcification having taken place.

Ascaris lumbricoides.—The round worm has been demonstrated in two cases by Otto Fritz, the worms being seen in the opaque meal.

In the light of recent work on the life history of the parasite, in which it has been shown that the embryos of the parasite pass to the liver and then to the lungs before reaching the intestine to become mature, it might be possible to demonstrate radiographic signs of the lung invasion in experimental animals.

The other helminthes found in man in this country do not produce any appearance which can be demonstrated by the X-ray except, perhaps, the *Bilharzia*. In some cases of this disease calcification of the bladder and ureter wall takes place. Lotsy has demonstrated the appearance so produced by the parasite.

Lastly, Köhler has demonstrated the radiographic appearance of infestation of the lung with *Paragonimus westermanii*.

BIBLIOGRAPHY.

- ALBERS-SCHÖNBERG, "Zur Röntgendiagnose der Lungenspitzenendiagnose," *Fort. a. d. Geb. d. Röntgenstr.*, v. "Beitrag zur Kasuistik des Lungenechinokokkus," *Fort. a. d. Geb. d. Röntgenstr.*, 1910, xvi, p. 290. ASSMANN, H., "Klinische Röntgendiagnostik der inneren Erkrankungen," 1924. BAUER, "Ein Fall von Echinokokkus der Tibia," *Fort. a. d. Geb. d. Röntgenstr.*, xix, p. 288. BEHRENSROTH, "Lungenechinokokkus," 8 Röntgenkongress, *Deutsch. med. Woch.*, 1913, xxxiv, p. 2287. BLES, "Ein Fall von Lungenechinokokkus," *Fort. a. d. Geb. d. Röntgenstr.*, xxiv, p. 319. BRAILSFORD, J. F., "The Life Histories of the Animal Parasites (Helminthes) found in Man in England," *Sanitary Journal*, March, 1914. BRUMPT, E., "Précis de Parasitologie," Paris, 1910. FISCHER, *Wien. med. Woch.*, 1912, lxii, p. 282. GEIPEL, "Cysticercus Cellulosa der Körpermuskulatur," *Fort. a. d. Geb. d. Röntgenstr.*, 1913, xx, p. 594. GRAHAM-SMITH, "Flies and Disease, Non-blood Sucking Flies," 1913. GUICHARD, "Zur Differentialdiagnose des Lungenechinokokkus," *Deutsch. med. Woch.*, 1913, xxxiv, p. 1938. HENNEBERG, R., "Über Gehirncysticerken, insbesondere d. basale Cysticerkenmeningitis," *Charité-Annalen*, 1906, xxx, p. 202. KARTULIS, "Ueber pathogenen Protozoen b. Menschen," *Zeitschr. f. Hyg. u. Infekt.*, 1893, xiii, p. 1. KÖHLER, "Zur Röntgendiagnose der Schmarotzer des Menschen (*Cysticercus cellulosa*, *Distomum pulmonale*)," KUHN, H., "Cysticercus Cellulosa in den Lungen," *Inaug.-Diss.*, Leipzig, 1905. LANDOIS, *Bresl. Chir. Geo. Sitz.*, vii. LEUCKART, R., "Die Parasiten des Menschen und die von ihnen herrührenden Krankheiten," 2nd ed., Leipzig, 1879. LEVY-DORN, "Trichinose im Röntgenbild," *Fort. a. d. Geb. d. Röntgenstr.*, 1923. LUHE, BRAUN, U., "Leitfaden zur Untersuchung der Tierischen Parasiten," 1908. MOLLOW, "Beitrag zur Röntgendiagnostik des Lungenu. Leberechinokokkus," *Fort. a. d. Geb. d. Röntgenstr.*, 1910, xv, p. 167. NEUMANN, L. G., "Traité de Parasitologie animale et végétale appliquée à la Médecine," Paris, 1896. NICOLL, W., "On the Part played by Flies in the Disposal of the Eggs of Parasitic Worms," *Reports to the Local Government Board on Public Health and Medical Subjects*, n.s., No. 53, 13-30 (1911). OSTERTAG, *Handbuch der Fleischbeschau*. OWEN, R., "Description of a Microscopical Entozoon infesting the Muscles of the Human

52 Brailsford: *The X-ray Diagnosis of Animal Parasites in Man*

Body," *Trans. Zool. Soc. Lond.*, 1885, i, p. 315. PICHLER, "Klinische Beobachtungen über Muskel- und Hautfinnen Röntgennachweis verkalteter Zystizerken," *Wiener klin. Woch.*, 1911. *Idem*, "Über die Verbreitung und Artbestimmung der Bandwürmer insobenderheit der *Taenia Solium*," *Fort. a. d. Geb. d. Röntgenstr.*, 1913, xx, p. 594. SAUPE, "Über den röntgenologischen Nachweis eines verkalkten *Cysticercus*," *Fort. a. d. Geb. d. Röntgenstr.*, xiii. SICK, *Deutsche med. Woch.*, 1905, p. 1294. STIEDER, "Verkalkte Parasiten (*Cysticercus Cellulosae*) im Röntgenbild," *Beitr. z. klin. Chir.*, xlii. VIALLET et RANDAVEL, "Les Kystes hydatiques calcifiés du Foie," *Journal de Radiol.*, November, 1923. VOLOVATZ, E., "Ladrerie ou cysticercose de l'homme," Thèse de Paris, 1902. WADSACK, "Ein solitärer Echinokokkus der linken Lunge durch Aushusten spontan geheilt," *Berl. klin. Woch.*, 1906, xliii, p. 1097. WEINBERG, "Zur Kenntnis des Lungenechinokokkus," *Fort. a. d. Geb. d. Röntgenstr.*, xxiv, p. 320. WEINBERGER, "Zur Diagnostik und Therapie intrathorakaler Zystensacke (Spontanheilung eines intrathorakalen Zystensackes, vermutlich Echinokokkus nach Probepunktion mit radioskopischen Befunden)," *Wiener Archiv f. klin. Med.*, vi. WILHELM, "Ein Fall von Lungenechinokokkus," *Fort. a. d. Geb. d. Röntgenstr.*, xxiv, p. 59. ZFHOE, "Lungen- u. Pleuraechinokokkus," *Fort. a. d. Geb. d. Röntgenstr.*, xxiv, p. 63. ZENKER, F. A., "Über die Trichinenkrankh. des Menschen," *Arch. f. path. Anat.*, 1860, xviii, p. 561.

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Diathermy in the Treatment of Pneumonia.

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HISTORY.

CREDIT for the earliest attempt to use diathermy in the treatment of pneumonia apparently belongs to two American workers, Frederick DeKraft and Byron Sprague Price, of New York, about the year 1906. The former confined his work to the attempt to obtain early resolution in several cases in which it was delayed, and in 1913 he gave instructions for its use on himself during a severe attack of lobar pneumonia. Dr. DeKraft later described symptomatic relief similar to that obtained in our own treated cases. Dr. Price treated a number of cases, diagnosed as pneumonia, by diathermy in conjunction with the superheated dry air oven bath for elimination, reporting the work in general terms in 1916. In none of this work was there any attempt to type the organism, obtain chest X-rays, or confirm the diagnosis other than clinically.

The writer was unaware that any work had been done on the subject when the logic of it first appealed to him in 1921. There was in that year a severe epidemic in the U.S. Marine Hospital 21, New York, which he attended in the capacity of consultant in physiotherapy. After a conference with the commanding officer, Colonel George B. Young, and his clinical staff, it was decided to try diathermy experimentally, upon our assurance that with careful technique it was reasonably safe. However, the institution of this experiment was postponed until we had a case in which we believed there was otherwise no possible chance of recovery. This case—that of a merchant seaman in the eleventh day of a creeping involvement of the lobes—was believed to be hopeless, and the patient's family had been so informed. He was given a through-and-through antero-posterior diathermy with bare composition metal plates, 2,000 ma. for twenty minutes. The result of this treatment was, indeed, beyond our most sanguine expectations. His clinical improvement was immediate and marked, and he made an uninterrupted recovery with subsequent treatments given twice daily.

It was realized that this result might have been accidental, but we were greatly encouraged to continue the work. In order to make our study of scientific value and justify its acceptance by the profession, the following plan was evolved. Each case was studied, written up, and checked by the medical staff. X-ray and laboratory reports were made by the regular staff, and no change from the usual medicinal, nursing and dietetic care of the patients was made. In our series of the next twenty cases so treated we had but one fatality, a case obviously moribund from the start.

It was the desire of the medical staff, after the results demonstrated in this preliminary series, to apply diathermy in every case as soon as the diagnosis was made. It was felt, however, that there was need for the study of a control group, so for the remainder of the season every third case was used as a control. The patients were chiefly all merchant seamen, whose age, alcoholic history, and conditions of life were practically identical. They were treated exactly alike from all standpoints except in regard to the use of diathermy. We had forty-one treated cases with a death-rate of 17 per cent., and twenty-one controls with a death-rate of 42½ per cent.

These results were published from time to time in various articles and in the author's book, "Diathermy with Special Reference to Pneumonia," Paul B. Hoeber, Inc., New York. This work led to the treatment of cases in private and hospital practice by quite a large number of

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individuals in our country. Among those who have reported the results are Granger, Brosier, Westervelt, Lacy, Otis, Walsh, Benson and Snow. So far the only record we have of a group of treated cases in Europe is that by Miller, in Schmidt's Clinic, at Prague. Several of these physicians also employed a reasonably long series of controls, and in each instance reduction in the mortality among the treated cases was significant.

TECHNIQUE.

Our technique has varied but little since it was first described in the writer's preliminary paper.

(a) *Electrodes.*—We use bare, flexible, metal electrodes, covered with a heavy shaving soap lather, placed directly on the skin, antero-posteriorly. In the treatment of a single lobe in an adult they are approximately 5 in. by 7 in. in area. For the treatment of two adjacent lobes the plates are about 6 in. by 8 in. Still larger plates may be used in an attempt to reach most of the area involved in a diffuse broncho-pneumonia. We have experimented to some extent with the interposition between the electrode and the skin of saline-soaked gauze or chamois leather, but have been unable to find any distinct advantage in the use of these substances. Flexible electrodes of German silver chain material have been used considerably, and are, theoretically, of advantage as the upper electrode, since they easily shape themselves to irregular contours of the chest. In practice, however, the difficulty of securely fastening the cord clips and the tendency for heat to accumulate near the clips constitute distinct disadvantages in their use.

On account of the difficulty in keeping the plates warm, it is well to have the cords already inserted in the D'Arsonval terminals and the electrodes prepared singly. The patient's back is bared with the least possible disturbance to him. The plate is immersed in hot water, and a rich, creamy, hot shaving soap lather prepared and applied to the electrode. By depressing the mattress, the posterior electrode, after being clipped on the cord, can be slipped under, to the proper position without necessitating the patient's turning. A folded bath towel or small pillow may then be crowded underneath to ensure good contact. The upper plate is similarly prepared, placed in position, and usually retained by the spread finger-tips of the operator, who then manipulates the apparatus with the free hand. Care must be taken not to place any weight on the anterior electrode. The patient should be encouraged to report any undue tingling or localized heat.

At first we experienced considerable trouble with the large spring clips, especially on the posterior electrode. There have now been developed types of flat clips that obviate this difficulty.

After the apparatus is turned on, four or five minutes are consumed in raising the current slowly and steadily to a maximum of 1,200 to 2,000 ma., as the state of the case demands.

(b) *Dosage.*—Our experience has demonstrated the advantage of giving, in general, longer treatments at less milliamperage; that is, instead of twenty minutes at 2,000 ma., we are now more likely to employ 1,200 to 1,400 ma. for thirty to forty minutes. In very severe cases I have not hesitated to use 2,400 ma. for an hour at hourly intervals, and this intensification has brought a few cases through in which the patients were not expected to live. Our longest treatment was six hours. In regard to frequency of application, our early reports were made in hospital practice, with limited apparatus and overworked personnel, so that two treatments daily was the maximum that could be given in any case. In private practice severe cases are treated about every four hours, the early morning treatment usually being omitted. Recent experience has seemed to confirm our conclusions of a year ago, that we could, and should, intensify in duration, dosage and frequency in any desperate case. What the maximum of such intensification is I am not yet prepared to say.

EFFECT UPON THE HEART.

The impression has steadily been gaining ground with us that it is advantageous when the cardiac area is included in the current pathway, as in the treatment of a lower left lobe involvement. Because of a contrary opinion expressed in an editorial last year in the *American Journal of Electrotherapeutics*, the writer stressed this point in a case report read before the American Academy of Physiotherapy. In the discussion of this paper no less than seven physicians agreed with my point of view, and several of them went so far as to give alternate treatments through the heart in cases in which it was not included in the treatment of the involved pulmonary area. The lateral through-and-through route was advocated in the

editorial cited, because by that method the greatest amount of heat was believed to pass behind the heart. A study of a cross-section of the chest would indicate that such bilateral applications would bring the greatest density of heat within the mediastinal space and not within any involved lobe, hence the antero-posterior route is by all means the better.

CLINICAL RESULTS.

Whilst our total case reports of between three hundred and four hundred are sufficient in number to answer certain questions that will arise in the clinician's mind, they are not sufficient to justify any dogmatic statements. These results, however, within their numerical limitations, have been quite uniform and may be summarized as follows:—

(a) *Temperature.*—There is a temperature drop by lysis in about 97 per cent. of the treated cases. Many times the temperature fall began as early as the second or third day. In about 1 per cent. of our cases, where it seemed that the reacting power of the patient was insufficient, diathermy led to a sharp rise in temperature, followed by a reduction by lysis, and a lessening of the pulse and respiratory rate as well. It is felt that this early reduction in temperature is a measure that conserves the body's energy, and therefore a definitely favourable factor.

(b) *Circulation.*—A lessening of cyanosis, whenever present, has been an almost invariable result of the treatment. This improvement is more marked when the left lower lobe is involved. We have explained this, first, by an increased respiratory excursion due to relief from pain, and secondly, by an improvement in the intrapulmonic circulation around the consolidated area. As cyanosis is an index of the load on the right ventricle, its relief must indicate a decrease in that load. There is usually some permanent decrease in the amount of cyanosis as the treatments progress. The pulse-rate falls slightly, as a rule, with marked improvement in the quality, especially where the pulse has been irregular and thready.

(c) *Respiration.*—The respiratory rate is lessened on an average by about five per minute, due, undoubtedly, to the above-mentioned factors of decreased pain and increased pulmonary circulation. In all but a few cases the typical "respiratory grunt" disappeared with the first treatment and never again occurred.

(d) *Pain.*—I believe that the depressant action of acute pain has never received proper emphasis in the literature on this disease. The improvement in respiration, the increased sleep, and the lessening of anxiety which follows the analgesic effect of diathermy, are factors of no small importance to the patient. In fact, this symptomatic relief which allows the patient to marshal his own resistive forces may often be sufficient to turn the balance in favour of recovery in a severe case. A sleep of from one to four hours following treatment is often the rule.

(e) *Extension.*—There has been additional pulmonary involvement in about the same proportion as is usual in untreated cases. Perhaps the latest development in technique has been to provide electrodes sufficiently large to ensure the application of the current to lung tissue adjacent to the involved area. The cases in which this method has been applied are yet too few for a definite statement as to results, but they indicate that the proportion of cases in which extension occurs may be greatly cut down by this method.

(f) *Perspiration.*—There is marked increase in the amount of perspiration after nearly every treatment. When not too profuse this is probably an aid in toxic elimination.

(g) *Complications.*—Apart from the matter of additional involvement just mentioned we have had a number of cases in which empyemas have developed. This has occurred in about two-thirds of the proportion we would expect in untreated cases. The systolic blood-pressure is lowered a few points, as a rule, during and immediately after treatment. At first we feared this effect in cases showing marked hypotension, but in the light of subsequent experience we believe the favourable effect of the diathermy more than counteracts this result.

(h) *Duration.*—It has been contended by some writers that the heat developed by diathermy has a bactericidal effect. Were that so we should expect a sudden termination of the disease when treatment was instituted. Such has not been the case in our experience.

(i) *Resolution.*—As might be expected, the central heat produced by diathermy hastens resolution. There were only one or two cases, complicated by slight degrees of tuberculosis, in which resolution was prolonged even under treatment. On the other hand, a few cases resolved, we thought, rather too quickly, with signs of toxic absorption, and here diathermy was immediately stopped.

(j) *Mortality.*—We must be extremely conservative in any statement regarding mortality. This is a disease in which the death-rate in different epidemics varies widely. Treatment

after treatment has been tried and abandoned. This much, however, can be said for diathermy. The death-rate has been about halved in four series of treated cases and controls in the hands of different men. In fact, in this connexion I am glad to state that several of my American confrères have obtained a lower mortality in their cases than I have in my own. This fact is gratifying because it indicates that results are not dependent upon any purely personal skill or technique, and that it should be possible to approximate them wherever the treatment is scientifically applied. The grand average death-rate is now twelve and nine-tenths per cent. This covers four years and includes many different seasonal epidemics and all types of the disease, including streptococcus pneumonia. No cases were refused even though apparently moribund, and every patient living long enough to receive the second treatment is included. About forty-two patients in our series are now living, for whom hope had been abandoned by the attending clinicians. In addition, it is from every point of view logical that the visible symptomatic improvement should have an indirect effect upon mortality. We do not, then, claim a reduced mortality due to diathermy, but all the evidence at hand points to the presumption of a decreased death-rate. In spite of the fact that in private practice, at least, this measure is often reserved for desperate cases, the mortality figures under its use are steadily decreasing. There are but two recorded deaths in the entire series in which diathermy was applied before the third day. When all the cases treated during the past winter are collected we hope to have a sufficient number on which to make a definite statement in regard to the death-rate.

SUMMARY.

In the proper application of diathermy to pneumonia we have an almost certain symptomatic aid for its employment as an adjunct in the patient's treatment régime. Cyanosis, pain, dyspnoea, and cardiac embarrassment are almost uniformly relieved and restful sleep induced. The most encouraging feature in our results has been the opinion of the value of the treatment expressed by some ninety clinicians who have closely followed their cases under treatment. Incidentally, the patients themselves, the technicians, and nurses in the cases, have been almost unanimous in their estimate of its value. The treatment seems, from every standpoint, to be a safe and conservative one. Not a single untoward result has followed the administration of over three thousand individual treatments, and only one death, which was obviously immediate, occurred under an attempted first treatment. The word "cure" is not used, or meant to be implied, in anything I have published on the subject.

CONCLUSIONS.

The writer finds it impossible to bring this paper to a close without expressing his keen appreciation of the honour accorded him by your invitation to address this Section. He is in the presence of members of the profession, one of whom has served as President of the American Electrotherapeutic Association, and many of whom are the authors of works which are eagerly welcomed by American specialists in this field. Work far superior to that here reported may have been done by Members of your Section. This report is made, however, in the hope that it may emphasize more strongly a type of treatment which we have begun to feel certain is helpful in this justly dreaded disease. We trust through your criticism and clinical observation of this subject greatly to extend our own knowledge and the value of this measure to the patients whom we serve.

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SECTION OF EPIDEMIOLOGY AND STATE MEDICINE.

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**SECTIONS OF BALNEOLOGY AND CLIMATOLOGY
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the views put forward in the various papers.

Section of Epidemiology and State Medicine.

President—Dr. JOHN C. McVAIL.

On the Management of Scarlatinal Epidemics in Schools and Institutions.

By T. STACEY WILSON, M.D. Edin., F.R.C.P. (Birmingham).

IN this communication I wish to bring forward some facts and suggestions which I hope may prove of service to those upon whom devolves the responsibility for the management of scarlatinal epidemics in schools and institutions.

The careful observation of many outbreaks of scarlatina in the Royal Institution for Deaf and Dumb Children, Edgbaston, of which I have been consulting physician for more than thirty years, has shown me that the task of dealing with such epidemics is complicated by certain difficulties which I propose to divide into two groups, namely:—

(1) *Difficulties due to the fact that the initial symptoms and signs of an attack of scarlet fever may be very slight, and not characteristic of the complaint, but may nevertheless be followed by desquamation, which is capable of infecting other children with unmistakable scarlet fever.*

(2) *Difficulties due to the fact that in very mild cases there may be no initial symptoms at all, and desquamation of an infective type may be the first and only evidence that the subject has had an attack of scarlet fever.*

Many minor difficulties are associated with the detection of scarlatinal desquamation in mild and symptomless cases.

(1) DIFFICULTIES DUE TO THE SLIGHTNESS OF THE INITIAL SYMPTOMS OF AN ATTACK OF SCARLET FEVER.

(a) *With regard to the Constitutional Symptoms.*—In mild scarlet fever a child when undoubtedly suffering from the complaint may, nevertheless, have only one out of the three or four symptoms which usually characterize an attack. For instance, a single attack of vomiting, and nothing else, or a few hours' headache and malaise, or a few hours of slight pyrexia—any one of these may be the only constitutional symptom present in the case of a child who afterwards desquamates and then becomes capable of infecting other children.

The following is an instance of what may happen. In the course of an epidemic in which it was found necessary to separate those children who were suffering from minor ailments that might have been really scarlet fever, four boys were isolated in a room by themselves; in one of them there was a slight rise in temperature, one had an attack of vomiting, two had had sore throats, which were not definitely scarlatinal. After about a fortnight's isolation, one of the four began to show a little desquamation on the soft skin of the hands, and he was immediately transferred to the fever hospital. That it was certainly scarlatinal desquamation was shown by the fact that within twenty-four hours of his removal one of his three companions developed a typical scarlatinal rash and sore throat, and also had to be sent to the fever hospital. Such a fact as this adds greatly to the difficulty of dealing with a scarlatinal epidemic, for the separation of all those who have minor ailments of this nature, and the keeping of them isolated for two or three weeks, is no easy task in a large institution.

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Fortunately, epidemics seem to vary somewhat, for it has not always proved necessary to take the extreme measures here mentioned, although occasionally it is not possible to control an epidemic until all cases of minor ailments are isolated.

(b) *With regard to the Rash.*—In mild cases of scarlet fever it is by no means very unusual to find that, instead of the usual punctiform rash, a slight blush is all that is observable, and the only feature which suggests that it is of the nature of a rash is that it spreads from place to place in a manner characteristic of a scarlatinal eruption. For instance, on examining a child complaining of a slight sore throat or headache, the lower part of the thigh may be noticed to be a little redder than the upper part, and on testing by pressure it is proved to be a definite blush. When the child is examined again in a few hours' time it is found that the blush has spread to the upper part of the thigh, the lower part being now paler than the upper part, and at the end of eight to twelve hours the blush may have left the thighs and be observable on the lower part of the abdomen. In the same way a blush noticeable on the arms may in a few hours travel on to the chest or neck.

The occurrence of such a travelling blush is practically certain evidence of scarlet fever, and should be carefully looked for in every case when, during an epidemic, a child suffers from some minor ailment which might possibly be the only representative of the usual initial manifestations of scarlet fever. It is well to remember that these blushes are often very evanescent, lasting as a rule only twelve hours or less.

(2) DIFFICULTIES DUE TO THE FACT THAT SCARLATINA MAY SHOW NO SYMPTOMS AT ALL PRIOR TO DESQUAMATION.

The chief difficulty in dealing with epidemics of scarlet fever is that an attack of fever which is so mild that there are no recognizable prodromal or initial symptoms whatever, may, nevertheless, be followed by desquamation which is sufficiently infective to give rise to a typical, or even a fatal, attack of scarlet fever.

It is not, I believe, as widely recognized as it should be that cases of scarlatina can be practically symptomless, so far as all manifestations preceding desquamation are concerned. I am, however, convinced (as the result of carefully watching many epidemics of scarlet fever) that such is the case, and I believe that anyone who periodically inspects the hands and feet of a large number of children during scarlatinal epidemics, as I have done, will receive convincing proof of the truth of this.

It was more than a quarter of a century ago that the possibility of scarlatina being practically symptomless in its early stages was first brought to my notice. On that occasion an epidemic of scarlet fever began in the middle of the spring term, and several cases occurred in which the possibility of infection by contact with a known case of scarlet fever could be excluded. I therefore suspected the presence of some child who was desquamating, and on inspecting the hands and feet of all the 160 children in the institute, I found a girl with typical scarlatinal desquamation, who during the six or eight weeks since the holidays had not been out of school for illness at all, and had made no complaint of any ailment. So far as my memory goes, in this instance the epidemic ceased on the isolation of this particular child, and of several others who were showing roughness of the feet and hands which might be of scarlatinal origin. In spite of the mildness of the attack from which this girl suffered, one of the girls who caught it from her had such a severe type of scarlatina that death ensued.

During the last twenty-five years I must have sent at least 30 or 40 children to the Scarlet Fever Hospital on account of desquamation without early symptoms, and I believe that in no instance did any of the children contract scarlet fever from the cases with whom they came in contact in the fever hospital.

On one occasion, many years ago, I had an experience which was of the nature of a "control experiment" in this connexion; for after a general inspection of the children and staff, I had isolated some eight or ten children who were showing

roughness of the hands and feet which, in the opinion of myself and my colleague the medical officer of the institution, was characteristic of scarlet fever. We also had isolated about the same number of children for further observation, in whom the roughness did not appear to be typical and whom we were not prepared to certify. As the suggestion was made that a third opinion might be desirable, the superintendent of the Scarlet Fever Hospital was asked to see the children concerned, and he decided to admit both the above groups to the hospital, with the result that while none of the first group whom we considered to be certifiable contracted scarlet fever in the hospital, two or three of the second group did so and suffered from typical attacks.

Confirmatory evidence of the point under discussion is also given by the fact that where cases of scarlet fever occurred which could not be accounted for by contact with recognizable cases, a general inspection never failed to reveal some children who were desquamating, and whose isolation, combined with periodic repetition of the inspection, usually sufficed to check the epidemic.

Absence of a Rash in Mild Scarlatina.—When speaking of all recognizable initial symptoms being absent in cases of very mild scarlatina, I am not bringing forward any evidence that there has never been any rash in these cases. It is not necessary for me to lay stress upon its absence, for in a large institution it would be practically impossible to detect a faint and evanescent rash on the body or limbs of a child, if it were unaccompanied by any symptoms which would make it desirable that the child should be carefully watched. I am quite prepared to believe that many of these children who are found to be desquamating may have had a slight rash in the early stage of their attack. I am, however, prepared to assert that in all probability some of them had no rash at all, and for the following reason:—

The careful inspection of children who have the complaint in such a mild form that they only suffer from some apparently minor ailment such as slight malaise, or a non-typical sore throat, will often (as has already been pointed out) reveal a slight blush on the limbs or body, which, though not typical in its appearance, must nevertheless be recognized as a modified form of rash because of the way in which it spreads from the limbs to the body. Now if the severity of the infection in these cases, although enough to *cause some constitutional symptoms*, is only enough to cause a very faint and barely recognizable skin eruption, we are certainly justified in believing that where the attack is so mild that there are *no constitutional symptoms at all*, it is in the highest degree probable that there will be no observable skin eruption.

We now have to deal with difficulties in the management of scarlatinal epidemics which are due to the occurrence of those cases where desquamation gives the only recognizable evidence of an attack of scarlet fever. The difficulties that have to be faced are mainly due to the slowness and to the evanescence of the desquamation. They are the following:—

DIFFICULTIES ASSOCIATED WITH THE RECOGNITION OF SCARLATINAL DESQUAMATION.

(1) *Due to the Slowness of the Desquamation and its Limitation to small Areas on the Hands and Feet.*—It would seem as if the virulence of the toxic agent which affects the skin was so low in these mild cases that it was only capable of causing exfoliation in situations where the epidermis was very thin or where, as between the toes, there was a natural tendency to desquamation.

In these cases we must not therefore expect to see large areas of desquamation, as in ordinary scarlet fever. Moreover, it is not likely to be visible where thin epidermis is exposed to the friction of the clothes, for the desquamating portions would be too readily broken away and rendered invisible.

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Desquamation of this type must be looked for only in those situations where thin epidermis passes more or less rapidly into epidermis of a thicker character, for in such places there is apt to be a ragged edge marking the boundary between the area which has desquamated and that which has not. Such situations occur on the hands and the feet. In the case of the hands, however, the friction to which they are exposed is liable to destroy evidences of this slight desquamation. Nevertheless, the hands should be examined, because evidences of desquamation may sometimes be detected along the outer border, where the thin epidermis which clothes this part passes into the thicker epidermis of the palm. Also where similar conditions occur between the fingers desquamation may sometimes be noticeable.

In the case of the feet there is not the same amount of friction, and it is here that desquamation in cases of mild scarlet fever must be looked for. The most likely situations are along the outer and the inner borders, from the heel to the metatarso-phalangeal joint, more especially along the edge of the thicker skin of the sole. Another likely situation is on the inner side of the great toe, where thin skin passes into the thicker skin which covers its plantar aspect.

Another situation where scarlatinal desquamation is recognizable is the space between the toes. Here, however, the diagnosis must rest not upon the presence of desquamation, because it is observable in very many normal feet, but it must rest upon its character, and more especially its rate of spread from day to day.

(2) *Due to the Character of the Desquamation.*—An essential feature of the scarlatinal eruption is its punctiform character. This feature is of much assistance in these mild cases, for the epidermis seems first to break over small circular areas $\frac{1}{16}$ to $\frac{1}{8}$ of an inch in diameter, and to give rise to the formation of small rings which look like small indistinct broken blisters. These small circular areas coalesce as the desquamation spreads, leaving an irregular edge which shows traces of the original circular breakings. The presence of even two or three such circles is strong evidence in favour of scarlatinal desquamation. Photographs of these are shown in figs. 1, 2, 3 and 4 (pp. 5, 6), and two cautions respecting them are referred to below.

When looking for evidences of scarlatinal desquamation in the soft and often sodden skin between the toes, it is not easy to be certain as to the nature of the desquamation. The points upon which stress can be laid are: (1) The presence of circular breaks in the skin, and especially their occurrence where the skin is not sodden; (2) the appearance of fresh circles from day to day, and the spread of the previously observed desquamation upward on to the dorsum of the toe, or downward on to the soft skin of its plantar aspect. In cases in which the desquamation is an ordinary characteristic of the child's feet it will remain practically unchanged from day to day, and will not invade the drier skin towards the dorsum of the toes.

Another point of importance is the appearance on successive days of circular breaks in the epidermis between toes which were free from desquamation when first inspected. As the skin between the fourth and fifth and third and fourth toes is normally more liable to desquamation than that between the others, it is here that punctiform desquamation is first likely to appear. Its subsequent appearance between the other toes is very suggestive of scarlet fever, *vide* (d).

(a) *The desquamation in these mild cases involves such a thin layer of epidermis that frequently it can only be clearly recognized for a short time after the hands or feet have been washed and dried.*

The action of the soap and water and the towel doubtless helps to intensify such roughness as exists.

(b) *The desquamation is sometimes so evanescent that weekly inspections of the children's hands and feet are desirable during an epidemic of scarlet fever.*

(c) *The somewhat prolonged soaking of the feet and hands which is inseparable from the inspection of a large number of children is apt, in certain cases, to cause a progressive desquamation which closely resembles that due to mild scarlatina.*



FIG. 1.—Scarlatinal desquamation. Boy isolated on November 14, 1923. Photograph taken on November 15. Outer side of left great toe showing two circular breakings on November 15, 1923.



FIG. 2.—Scarlatinal desquamation. Boy isolated for desquamation, November 14, 1923. Circular breakings seen under fourth right toe. Photograph November 16, 1923.

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An unaccustomed amount of washing seems to be very liable to cause desquamation of children's feet, and I believe that when children are used to running about barefooted, and have very little to do with soap and water, the introduction to it, when they are admitted to hospital for any cause, frequently produces very copious desquamation.

In an institution in which 150 children have to be inspected within the course of two or three hours, it is almost unavoidable that their hands and feet should remain wet for some time prior to their coming up in turn for inspection. There is no



FIG. 3.—Scarlatinal desquamation. Outer side of left heel showing ragged edge of skin.



FIG. 4.—Scarlatinal desquamation. Outer side of right heel showing circular breakings not visible on previous day.

doubt that the weekly recurrence of this unusual amount of washing of the feet does, in the case of some few children, induce desquamation which, in its character and progress, may sometimes so closely resemble that of scarlet fever that there seems to be no certain way of distinguishing it.

There is, so far as I know at present, only one way of meeting this difficulty, and that is by isolating such children and treating them as suspicious cases. By doing

so there is some risk that the cases which are spurious may be infected by those which are true scarlatinal desquamation, but this is a lesser evil than leaving all such cases in contact with the healthy children. If this latter course be adopted there will be little chance of controlling an epidemic of scarlet fever until all the susceptible children have caught the complaint.

(d) *Certain children are constitutionally liable to a form of desquamation of the feet which, though quite distinct when once recognized, might without due care be mistaken for that of scarlatinal origin.*

TYPES OF DESQUAMATION SIMULATING THAT DUE TO SCARLET FEVER.

I have met with three distinct types of desquamation which may simulate that due to scarlet fever.

(1) In the first place it seems as if, in some children, the normal desquamation took place occasionally by means of circular breakings away of the epidermis just as is the case in mild scarlet fever. Such cases are recognizable by the fact that the circular areas of desquamation do not increase in size from day to day, as is the case

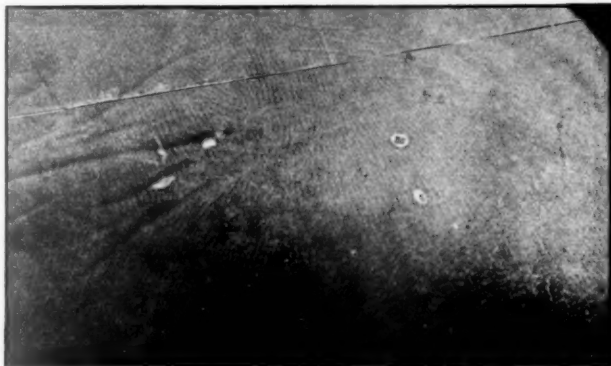


FIG. 5.—Non-scarlatinal desquamation in a girl who had scarlet fever two years ago. Inner side of right heel showing circular breakings characteristic of scarlet fever, but non-progressive.

with an infective desquamation. During the November epidemic, 1923, a girl was isolated who showed some circular breakings on the heel exactly like those shown in fig. 5. She had had scarlet fever twelve months previously, and these circular areas of desquamation remained stationary in size for several days.

(2) There is a type of irregularity of the epidermis almost worthy of being called a skin eruption, which is sometimes met with on the soles of the feet. This consists of numerous small circular areas of roughness, and often of pitting. They are easily distinguished from scarlatinal desquamation by their uniformity in size and by their non-progressive character. The roughened edges of the circular breakings are often darkened by dirt, this showing that they have been in existence unchanged in size for some days—a feature not noticeable in scarlatinal desquamation. In addition, the circular areas are far more numerous, and more evenly distributed, than is the case with scarlatinal desquamation (fig. 6, p. 8).

(3) Occasionally children are met with who, normally, seem to desquamate with the freedom characteristic of ordinary typical scarlet fever. There are usually one or two children whose feet are always desquamating more or less all the time (several years) that they are inmates of the institution.

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Of all these difficulties the most serious is that desquamation, sometimes indistinguishable from that due to very mild and symptomless scarlet fever, may be induced in some children by the weekly washing and somewhat prolonged soaking of the feet which is almost unavoidable when the feet of 150 children have to be examined every six or seven days.

Nevertheless, an occasional mistake does not detract from the value of the routine inspection of the children's hands and feet during the prevalence of an epidemic. For I believe that this is one of the most important means at our disposal for checking a scarlet fever epidemic in an institution.

AN ILLUSTRATION SCARLATINAL EPIDEMIC.

The difficulties associated with the diagnosis of scarlet fever are very well illustrated by an epidemic which occurred in October and November, 1923, at the Edgbaston institution.

The first case occurred on October 7, and was followed by two "contact" cases; then a girl was found to be desquamating, and it seemed probable that she was the

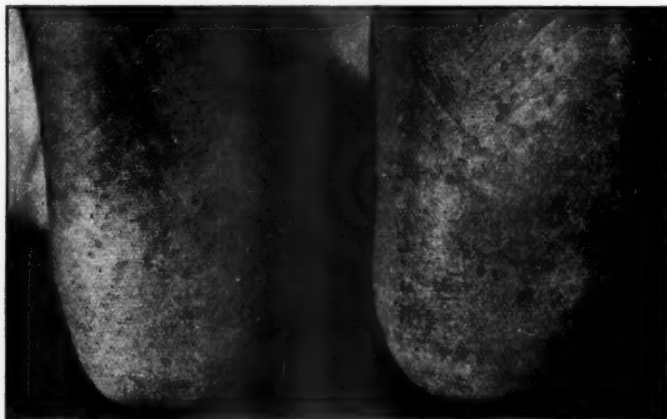


FIG. 6.—Non-scarlatinal desquamation. Punctiform, non-progressive desquamation of the soles of the feet. A chronic, symptomless condition of occasional occurrence.

cause of the epidemic. Several other cases occurred, and in some of them no "contact" was traceable.

It was therefore decided to inspect the hands and feet of all the children and the staff. This was done on November 14, and five boys and six girls were isolated for desquamation which appeared to be truly scarlatinal in nature. The desquamation ran a more or less similar course in all of them, and the girls were twice exposed to scarlatinal infection without being infected.

In addition, three girls and one boy were isolated who developed typical scarlatina during isolation, thus showing that the desquamation was non-scarlatinal.

At a second general inspection on November 20, a boy was isolated for progressive desquamation of his feet, of a type suggestive of scarlatina. He, however, developed scarlet fever three weeks later (after his return to school), thus proving that the desquamation was non-scarlatinal. It was almost certainly due to the soaking of his feet at the first inspection on November 14. No true cases of scarlatinal desquamation were detected at this inspection or at the following ones on November 26 and 30.

Within four days of the first inspection five cases of scarlet fever occurred; during the next week there was only one case. On the day after the third inspection there were two cases, followed by a "contact" case, and the final cases were two which occurred about December 6 and one on the 19th.

The fact that during the first four days following the first inspection there were six cases of scarlet fever, and then no other case for a week, seems to show the beneficial result of isolating the desquamating children. In the course of the next fortnight six children developed the complaint, and this was practically the end of the epidemic, which had involved thirty-seven children out of 150.

A Transient Spreading Blush in place of a Rash.

This epidemic gave two instances of a spreading blush; one of them was as follows:—

Two cases of scarlatina developed amongst the children isolated for observation within three or four days of the first inspection. Both these cases may have been due either to infection, preceding the inspection, by some of the cases of true scarlatinal desquamation, or to contact with one of the desquamating cases which were isolated. One of these well illustrated the occurrence of a spreading blush in place of a rash.

One morning, after being isolated three days, a boy was noticed to have a faint blush over the lower third of the left upper arm. Early in the afternoon this part of the arm showed no blush on testing by pressure with the finger-tip, but there was a distinct blush over the upper part of the forearm. By about six o'clock a slight blush was noticeable on the chest for the first time, and by the next morning all trace of a blush had gone, but the boy had a characteristic tongue and was transferred to the fever hospital. He had no other symptoms or signs of scarlatina, and no trace of any true punctiform rash.

In addition to these children who were isolated on suspicion, cases of spurious desquamation were found.

(1) There was a boy who in previous inspections during the last few years has been recognized as usually having desquamation of his feet.

(2) A girl was found with small circular breakings on the heels which were proved to be non-scarlatinal by the fact that they did not materially increase in size from day to day; moreover, she had had scarlatina a year ago.

(3) There were one or two cases in which the children were known to be liable to the kind of punctiform desquamation involving mainly the soles of the feet; this has been previously referred to.

SUMMARY.

(1) The main difficulty in dealing with scarlatinal epidemics depends upon the fact that mild cases of the complaint often occur in which there are no characteristic symptoms or signs preceding the occurrence of an infective desquamation.

(2) Therefore, whenever, in an epidemic, cases occur in which no contact with a previous case can be established, the presence must be suspected of someone suffering from scarlatinal desquamation without having had any recognizable signs of the complaint.

(3) When this occurs inspection of the hands and feet of all inmates is called for.

(4) To be effective the inspection must be repeated every six or seven days.

(5) As the desquamation is very slight in these cases, not only must the inspection be made in a good light, but the hands and feet must be seen immediately after washing and before the skin has completely dried.

(6) Progressive desquamation (which is non-scarlatinal) may be produced in certain children by the somewhat prolonged soaking of the feet which is necessitated by the inspection of a large number of children. This desquamation may be indistinguishable from that due to scarlet fever, and the risk must be run of isolating these children along with the scarlatinal cases.

(7) Other types of non-scarlatinal desquamation must be recognized.

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(8) When, in an epidemic, careful isolation of evident cases, and careful inspection of the children's hands and feet, do not suffice to stop the epidemic, all cases in which the patients are suffering from minor ailments which might be of scarlatinal origin (such as an attack of vomiting, sore throat, malaise, &c.) must be isolated and watched for two weeks or so, in order that it may be seen whether desquamation occurs.

CONCLUSION.

It may be stated by the medical officers of other institutions that they have not been faced by the problems here discussed. In answer to this it must be pointed out that two factors increase the liability to epidemics in this institution.

In the first place many of the deaf mutes are children of low vitality. A considerable number of them are much under weight when first admitted and need special dieting.

In the second place the institution has always drawn its children from all over the country, and the more so since the Birmingham School Authority decided upon day schools rather than institutional training for the City's deaf mutes. This custom not only increases the liability to the importation of infection, but may also introduce children to a type of the complaint to which they are more liable than to that prevalent in their native town.

That there is some truth in this last supposition is shown by the following fact: The Birmingham Institution for the Blind, which is also a residential one and draws its inmates from the Birmingham district, is situated within 200 yards of the Deaf and Dumb Institution which has been referred to. Nevertheless, this Blind Asylum has been very much less troubled with scarlatinal epidemics than is the case with the Deaf and Dumb Institution.

For the excellent photographs I am indebted to the skill of Mr. Benjamin Moor, one of the senior teachers at our institution.

Discussion.—Dr. E. W. GOODALL prefaced his remarks by stating that it had to be remembered that any observations he was about to make were based upon an experience of a hospital population which was constantly changing, whereas Dr. Wilson had been dealing with a fairly constant population. Thus Dr. Wilson had been able to observe the same children over a number of years.

That scarlet fever could occur without a rash had been known for a very long time. The absence of a rash was most frequent in the mild cases, but it might occur in the most severe cases, especially those of the anginous form. At the present time scarlet fever was a most difficult disease to diagnose, in many instances because of the absence or transient character of the rash and because there was no symptom which, taken by itself, was absolutely pathognomonic of the disease. The ringed or pin-hole desquamation described by Dr. Wilson might occur after any erythema, but was most common in scarlet fever. He did not agree that the occurrence of peeling of the hands and feet, or indeed anywhere, was necessarily diagnostic of scarlet fever, and he was very chary of sending into a scarlet fever ward any patient simply because that patient was peeling, unless he had clear evidence from some person who could be relied upon that other symptoms of scarlet fever had recently been observed. He was surprised to hear that Dr. Wilson was of opinion that the late desquamation was infectious. He thought that opinion had been abandoned long ago. It certainly had been given up by the majority of medical officers of health and superintendents of fever hospitals. During the past twenty-three years he (the speaker) had discharged thousands of scarlet fever patients after four or more weeks' detention in hospital who were peeling freely on the feet and legs, and the return case-rate did not appear to have increased through that procedure. Recent bacteriological evidence went to show that scarlet fever was, like diphtheria, in the first instance a local disease of the nose and fauces, and that the constitutional symptoms and the rash were due to the toxin which was absorbed from that region. It was improbable that the micro-organisms got into the skin. Further, clinical evidence went to show that in those cases in which the patient apparently remained infectious for some weeks after an attack, the infective agent remained active in the nose and throat. He was not impressed by the details of the outbreak of scarlet fever that Dr. Wilson had shown on the screen, nor did he think

that the outbreak had been checked by the minute inspections of the children in the school. It appeared to him that the outbreak had run a course which was usual in such circumstances. He believed that the control of epidemics in the future lay in the recognition of susceptible persons by means of the Dick test and the immunizing of them by a protective serum or a toxin-antitoxin mixture.

Sir JOHN BROADBENT said that he agreed with the view of Dr. Goodall that desquamation was not the source of infection in scarlet fever. Desquamation was only of importance in that the desquamating patient might be a carrier. He believed that the infection was latent in the throat, as in diphtheria, and that it was conveyed by throat carriers in the same way. It was impossible to say exactly when a scarlet fever patient ceased to be infectious; probably it was less than six weeks in the majority of cases, but in carriers it might be much longer. He narrated the case of a child who was admitted to the London Fever Hospital with a well-marked attack of scarlet fever. She was kept in for six weeks and had no complications. When she left all traces of desquamation had disappeared; there was no discharge from nose or ears, the throat appeared quite healthy, and the child was very well. Two weeks after discharge from hospital she went to stay with two aunts. They both contracted scarlet fever and one died. She then went home, and six weeks from the date of her discharge from hospital her small brother came home from school for the week end. He also contracted scarlet fever. No doubt this girl was a throat carrier. In the great majority of cases admitted to a fever hospital, there was no history of any source of infection, and probably it was conveyed by throat carriers or mild undiagnosed cases. As a result of the Dicks' work in America, he hoped that in the near future throat carriers in scarlet fever might be detected by a bacteriological examination, as in diphtheria.

Dr. Goodall had said that reliance could not be placed on the appearance of the tongue in scarlet fever, as the appearance of the tongue in measles was often very similar, but he (Sir John) considered that the peeling tongue of scarlet fever was of very great help in differential diagnosis, and there was seldom any difficulty in distinguishing measles from scarlet fever.

He had found the Schultz-Charlton blanching test—produced by the serum of immunized horses—of help in many cases in identifying the rash of scarlet fever, though sometimes blanching did not occur in apparently typical cases. Thanks to the courtesy of Dr. O'Brien, who had sent a supply of toxin and serum to the London Fever Hospital, Dr. Back, his resident medical officer there, had been able to carry out a series of Dick tests. He thought that the future of preventive measures in an outbreak of scarlet fever at an institution would lie in the application of the Dick tests of susceptibility and methods of immunization, but there were still difficulties in regard to standardization of toxins, appropriate dosage, and preparation of serum which had to be surmounted before complete reliance could be placed on them.

Dr. R. A. O'BRIEN said that in a school such as that described, immunological methods would probably be of real assistance, and observations of value could be made. If such a population were tested by the Dick method and the test repeated periodically, e.g., every six or twelve months, it would soon be possible to say whether a negative response to the test applied under these circumstances did indicate immunity from attack during natural epidemics. It was, of course, practically certain that it would indicate immunity, but we had not yet accumulated in England sufficient observations to tell us exactly what degree of protection was indicated by a negative response. Such a record would also help when an epidemic came, for, in the light of present knowledge, it would be reasonable to release all the negative reactors from observation and concentrate attention on the positive reactors. If the type of disease were severe, the positive reactors in contact with the patients could be passively protected with serum; if it were mild they could be observed from day to day and isolated on the first sign of any disturbance of normal health.

If the Dick test response of the children described with slight desquamation were known it might give some help. If a large number of such children changed in reaction from positive to negative within a few weeks, such evidence would go far to prove that these children had had an attack of scarlet fever.

We did not yet know with much accuracy how long the hæmolytic streptococci persisted in the throats of patients convalescent after scarlet fever. It was conceivable that some day we might have sufficiently definite knowledge to be able to say that a convalescent scarlet fever patient with hæmolytic streptococci in his throat was or was not a safe person to discharge into the general community.

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Dr. S. MONCKTON COPEMAN, while disclaiming expert clinical knowledge in connexion with scarlet fever, agreed as to the difficulties often met with in diagnosis nowadays, owing largely to the marked change in type of the disease that had occurred during the past half century or less. The recent researches of the Dicks, of Dochez, and others, in America, extended by numerous observers in this and other countries, had, however, afforded valuable assistance in this direction. Even though we might not as yet be prepared to accept, without reservation, the view that the specific micro-organism of scarlet fever was a streptococcus of the hæmolytic type, nevertheless the Dick test, consisting in the intradermal injection of a special streptococcus toxin, was undoubtedly capable of affording evidence as to susceptibility or the reverse to attack by scarlet fever. And, consequently, if a patient was known to have given a negative reaction to this test, it might be taken as practically certain that a subsequently occurring erythematous rash was not due to scarlet fever. Evidence on this point could also be obtained in doubtful cases by the inoculation of the streptococcus antitoxin into an erythematous area of the skin, when, if the rash were due to scarlet fever, a whitish patch would develop in the course of an hour or so—the so-called Schultz-Charlton reaction. In the event of the rash *not* being due to scarlet fever, no such reaction would be observed. The routine use of this test in cases of doubtful diagnosis would be likely to diminish the possibility of patients, not actually suffering from scarlet fever, subsequently contracting the disease in consequence of having been warned, by mistake, with cases of scarlet fever.

Dr. GRAHAM FORBES remarked on the difficulties attending the recognition of mild scarlet fever cases in the course of medical inspection in the elementary schools, where a prompt decision had to be made and daily observation of the progress of desquamation in a suspected case was not possible. Exclusion from school might be held advisable, even though it was realized that there was little risk of infection spreading as the result of continued attendance. It was not uncommon to find pin-point circular desquamation on children's hands quite independently of scarlet fever, but the areas were more often clearly defined by engrained dirt and thus distinguishable from the clean, fresh edging of true scarlatinal peeling. It had long been generally accepted that the stage of desquamation was non-infective, and that, provided the condition of the throat, nose and ears appeared healthy, there was no real danger to be feared from contact with cases which showed no other evidence of scarlet fever than that of peeling.

Dr. G. CLARK TROTTER complimented Dr. Stacey Wilson on the photographs which had been shown. These photographs of desquamation were not easy to take, they had to be very carefully produced in order to show the pin-point character of the eruption, and it required much patience and perseverance to obtain a good photograph, not to speak of the time required.

Regarding desquamation, it was apt to be very deceptive. He had in mind a particular case in which a child had suspicious desquamation on the hands, and after very thorough investigation it was found that that child had been playing with lime at a place where some buildings were being erected. Desquamation he believed to be non-infective. During an extensive outbreak of scarlet fever in Paisley, caused by mild, undiagnosed cases, the hospital accommodation was so severely taxed that it was resolved to provide the greatest benefit to the greatest number. The length of stay in hospital of cases free from inflammation, or discharge from the mucous membranes, was limited to four weeks. He had made a very careful comparison between the number of probable return cases under this system, and that in previous years, and had found that the results of the short stay were amply justified, there being actually fewer so-called return cases.

Infection took place by discharge from the ear and nose, or the mucous membrane of the mouth. It was unfortunate that in London cases occurring in homes immediately consequent on a case returned home from hospital were not adequately brought to the notice of the superintendent of the hospital from which the first case had been discharged. He made it a practice, when such came to his notice in Islington, to let the superintendents know; this was only fair if an endeavour was to be made to prevent such occurrences.

One of the most difficult cases he had recently to diagnose was the occurrence of scarlet fever in a half-caste.

Dr. STACEY WILSON briefly replied.

Section of Epidemiology and State Medicine.

President—Dr. JOHN C. McVAIL.

National Death-rates in Relation to National Differences in Methods of Housing.

By A. K. CHALMERS, M.D.

(Formerly Medical Officer of Health, Glasgow.)

INTRODUCTORY.

It was explained that the following inquiry had been undertaken with the object of ascertaining whether national statistics afforded any answer to the question whether the "cottage" and "tenement" type of house (using the latter term as synonymous with the "land of houses" as understood in Scotland) affected the health of the occupier in opposite directions.

The results were submitted to a conference of medical officers of health held during the Congress of the Royal Sanitary Institute in July last. The principal conclusion suggested is that the "tenement" system, as known in Scotland, is prejudicial to child life mainly through the commoner forms of infectious disease, and that the unabated continuance of these diseases, during a period in which the diarrhoeal death-rate among infants had undergone a marked diminution in England, goes far to explain the reversed relationship now existing between the infant mortality rates of both countries.

For this reason, and because of the economic issues implied in any suggestion that our national housing customs require reconsideration, a renewed criticism of the data on which the conclusion rests seems in the highest degree desirable; and so I have been induced to submit for your consideration material which, in view of what I have just stated, is not new.

Of recent years, and very largely in connexion with housing schemes, there has been, I think, a marked tendency in Scotland to get away from our former habit of building houses in tenements in favour of one which takes the cottage as the type, but modifies it on occasion, to provide four houses in one block, so arranged that each house has a separate entrance from the open air.

In England, on the other hand, if I understand the position rightly, there would appear to be a growing volume of opinion in the opposite direction—that is, in favour of the tenement type—so that each country would appear to seek a solution of its housing problem in the direction in which it has least experience.

How far the tendency in either case has been influenced by the amount of suitable and convenient building land available, or the economic bearing of this on the relative cost of site, has, of course, an important bearing on the question, but is not here at issue.

Primarily the question is whether the close proximity of tenement life creates conditions prejudicial to the health of the inhabitants which are absent from the cottage type of house. At first sight the question seems simple enough, and comparisons have been made between contrasted groups. But the accidents of selection are not inconsiderable and may vitiate the comparison, and it occurred to me that we have readily available a mass of information in our national statistics which may be applied experimentally, at least, to the question we propose to consider.

HOUSING CONTRASTS.

As illustrative of housing provision in England we may take, I think, Dr. Niven's description of Manchester as a city of cottages of four or five or more rooms.

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In Scotland, on the other hand, and more particularly in its urban areas, it is our habit to build tenements in blocks of three or four—sometimes more—stories in height, with two or three houses on each floor in modern tenements, four and even more in tenements of older type, especially where these have been “made down” from houses of larger size. Each floor is entered from a landing which is usually reached through a close or covered passage leading to an inside stair common to all the houses, so that few of our tenement houses save those on the ground floor enter directly from the open air.

At the outset, therefore, one important difference is obvious. The cottage type of house enters directly from the open air whether it be street or court; the tenement house as a rule enters from a contained space, whether it be close or stair, the air of which has free access to all the houses. The facilities which this offers to the transmission of certain forms of infectious disease we shall see later.¹

Another element in this picture is that at last census 72 per cent. of the population of Scotland were resident in houses of not more than three apartments, and 43 per cent. were living more than two persons per room.

Our houses have fewer rooms, but on the average the rooms are somewhat larger than those of houses in England.

GENERAL DEATH RATE.

On the basis of this housing contrast we may look cursorily at the crude death-rates of both countries.

Since 1861, in one decade only (1881-90), has this rate for Scotland been as low as that for England and Wales—usually it is fully 1 per 1,000 higher. In the decade 1871-80, and again in 1901-10, the excess was 2 per 1,000. This makes no correction for age or sex.

The groupings under which the excess rates in Scotland occur are the following:—

1 to 9. INFECTIOUS DISEASES, including influenza and infectious diseases of central nervous system.

11. TUBERCLE (other than lungs). (19) Pneumonia (all forms). (20) Other respiratory diseases.

12. MALIGNANT DISEASE (cancer). (21) Ulcers of stomach and duodenum.

15. CEREBRAL HÆMORRHAGE but not (16) heart disease. (25) Acute and chronic nephritis. (17) Arterio-sclerosis.

22. DIARRHŒA at “All Ages” save in “Northern Counties,” where at ages 1 to 5 it is higher than Scotland. Under 1 the rate for Scotland is much below the rate for England and Wales and for the Northern Counties.

23. APPENDICITIS and TYPHLITIS.

28. MALFORMATIONS.

DEATH-RATES CORRECTED FOR AGE AND SEX.

To extend the comparison into age and sex, I have taken out the deaths of each sex in eight age-groups for the years 1921-23, and applied them to the populations at corresponding ages of the County groups which I have obtained through the courtesy of the Registrar-General for England.

The northern boundary of the Midland Counties group would be represented by a line drawn irregularly across England from the Dee to the Humber along the southern limits of Cheshire and Yorkshire; and a second line, stretching from the Thames to the Severn and including London, separates the Midland from the Southern Counties. It is thus possible to compare the geographical divisions of England with Scotland as a whole.

I have grouped the deaths under thirty-two classes, but there are many difficulties in making a reliable comparison, especially when a second physiological system

¹Dr. Adam, Medical Officer of Health, Stirlingshire, has directed attention to the greater incidence of measles in urban than in rural areas in Scotland.

becomes involved before death. Probably the most frequent illustrations arise when heart disease of some duration proves fatal through a lung affection. In England, unless I am mistaken, this would be classified under heart disease, in Scotland under diseases of the respiratory organs. A system of national statistics should aim at least at uniformity. This difficulty does not arise, however, with deaths from infectious disease, but must be kept in view when making other comparisons.

The climatic differences of these geographical units may be represented thus:—

TABLE I.—TEMPERATURE AND RAINFALL.

	Mean temperature	Mean daily range	Rainfall in inches	Physical features
Scotland	47·9	13·3	39	Hilly
Northern Counties	49·6	13·6	26	Hilly
Midland	50·8	16·1	17	—
Wales and Monmouth	51·3	13·2	27	Hilly
Southern Counties	51·8	15·1	16	—

Note.—(1) The mean temperature rises steadily southwards; (2) the rainfall is dominated by the hills; (3) the daily range of temperature is uniform in the hilly districts, and greatest where there are no hills.

THE LIVES AT RISK.

The estimated population of England and Wales in 1922 was 38,158,000, and of Scotland 4,904,000, so that the lives at risk in both countries during 1921-23 amounted to over 129,000,000 (129,187,769), and the total deaths occurring among them to fully one million and a half (1,592,592). This would give a death-rate for Great Britain of 12·3 per 1,000.

For comparison these may be separated into the geographical groups just mentioned.

The population of these divisions in 1922 was as follows:—

TABLE II.

	Population
Northern Counties	12,867,591
Midland "	12,068,658
Southern "	10,535,629
Wales and Monmouth	2,686,123
ENGLAND AND WALES	38,158,001
SCOTLAND	4,904,456
	43,062,457

TABLE III.—LIVES AT RISK AND DEATHS IN GEOGRAPHICAL GROUPS (1921-23).

	Lives at risk (millions)	Deaths (thousands)	Average annual death- rate per 1,000
<i>England and Wales:—</i>			
Northern Counties	38·6	501	12·9
Midland "	36·2	412	11·4
Southern "	31·6	377	11·9
Wales and Monmouth	8·0	98	12·2
ENGLAND AND WALES	114·4	1,388	12·1
SCOTLAND	14·7	202	13·7

The following table shows that for each sex at all ages corresponding differences exist:—

TABLE IV.—THE DEATH-RATE AT ALL AGES. ALL CAUSES.

	Persons	Males	Females
SCOTLAND	13,756	14,278	13,273
Northern Counties	12,984	13,927	12,112
Wales and Monmouth	12,206	12,825	11,585
ENGLAND AND WALES	12,144	12,970	11,390
Southern Counties	11,915	12,757	11,184
Midland "	11,387	12,058	10,770

The extended tables of the causes of death at the eight age-groups extracted are not reproduced, but the following abstract of the rates per million for all causes at these age-periods will serve to indicate the contrast.

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TABLE V.—AVERAGE ANNUAL DEATH-RATE PER MILLION IN AGE-GROUPS FROM ALL CAUSES (1921-23).

Males									
Age-period	Scotland	England and Wales	Midland Counties	Southern Counties	Wales and Monmouth	Northern Counties			
0-1 ...	105,741	86,329	77,349	72,441	91,990	103,177			
1-5 ...	16,242	11,711	9,414	9,968	10,522	15,391			
5-15 ...	2,267	2,075	1,836	1,971	2,165	2,358			
15-25 ...	3,226	3,150	2,803	2,836	3,601	3,424			
25-45 ...	5,581	5,316	4,809	5,009	5,586	5,772			
45-65 ...	18,172	17,006	15,165	16,754	17,492	18,813			
65-75 ...	62,715	58,667	53,712	54,633	61,263	67,562			
75- ...	156,492	148,854	144,413	144,137	149,922	161,852			
All ages ...	14,278	12,970	12,058	12,757	12,825	13,927			
Females									
0-1 ...	80,437	65,555	58,409	54,818	70,900	78,599			
1-5 ...	14,937	10,820	8,868	9,195	9,602	14,068			
5-15 ...	2,245	2,038	1,827	1,955	2,167	2,269			
15-25 ...	3,262	2,844	2,689	2,578	3,706	3,026			
25-45 ...	5,181	4,340	4,027	3,927	5,259	4,806			
45-65 ...	14,910	12,994	11,796	12,045	14,099	14,825			
65-75 ...	49,841	45,962	42,106	41,469	48,825	54,640			
75- ...	136,192	130,124	125,999	124,129	136,197	143,827			
All ages ...	13,273	11,390	10,770	11,184	11,585	12,112			
Both Sexes									
All ages ...	13,756	12,144	11,387	11,915	12,206	12,984			

At "All Ages" and for each sex the death-rate from all causes in Scotland is thus appreciably in excess of each of the four groups of counties into which England and Wales is divided, and at each of the eight age-periods which have been taken the death-rate from all causes of the Midland and Southern groups is uniformly lower than in Scotland.

The Northern Counties, with Wales and Monmouth, show certain excesses. For example, in the Northern Counties the male death-rate from all causes exceeds that of Scotland at each age-period above 5 years, and the female death-rate at the age-periods 5 to 15 and from 65 onwards.

Some causes of excess in the Northern Counties are possibly inconstant, e.g., influenza and pneumonia, which yield higher rates at ages 5 to 75 among males. Rheumatic fever and heart disease are also in excess throughout the same ages, and arteriosclerosis from 45 to 75. But there is also more enteric fever after 15 and an excess rate from tuberculosis of the respiratory system from 5 years onwards.

In Wales and Monmouth again, the death-rate of each sex is higher at the ages 15 to 25.

SOME OF THE DISEASES WHICH YIELD HIGHER DEATH-RATES IN SCOTLAND.

In reviewing the tables on which these notes are based, the higher rate in Scotland at once arrests attention. Confining our scrutiny still to *all ages*, we have the following contrasts:—

TABLE VI.—THE INFECTIOUS DISEASES AT ALL AGES. DEATH-RATE PER MILLION.

	Scotland									
	England and Wales	Northern Counties	Wales and Monmouth	Southern Counties	Midland Counties					
1. Enteric fever ...	16	13	17	13	12	10				
2. Small-pox ...	2	—	—	—	1	—				
3. Measles ...	277	116	168	101	93	83				
4. Scarlet fever ...	59	32	38	35	33	25				
5. Whooping-cough ...	263	132	167	144	108	113				
6. Diphtheria ...	111	101	75	119	136	94				
	728	394	465	412	383	325				
7. Influenza ...	378	340	379	378	316	310				
8. Encephalitis lethargica ...	16	14	14	12	14	14				
9. Cerebro-spinal fever ...	22	9	9	7	11	8				
	416	363	402	397	341	332				
10. Tuberculosis of respiratory system ...	817	869	906	940	886	792				
11. Other tuberculosis ...	361	233	287	246	197	204				
	1,178	1,102	1,193	1,186	1,083	996				
1 to 11 ...	2,322	1,859	2,060	1,995	1,807	1,653				

For the commoner infectious diseases the excess in Scotland is marked. For scarlet fever, but particularly for measles and whooping-cough, the rate in Scotland is much above those for all the districts in England. This is not special to the selected years, as we shall see afterwards. For diseases of the central nervous system the rate in Scotland still leads. The lower phthisis rate in Scotland is in marked contrast with the rate from other forms of tuberculosis.

Our comparison so far has shown that for *each sex at ages under 5, and for "All Ages"* the death-rate of Scotland exceeds that of England and Wales as a whole, and also those of its several divisions; further, that in the Midland and Southern Counties, the population of which exceeds $22\frac{1}{2}$ millions, the death-rate of the sexes at each age-period is lower, and especially in the earlier ages much lower than the corresponding rates for Scotland.

Ages 0 to 5.

The causes of the difference at ages 0 to 5 years thus become of importance, because the rate is uniformly higher in Scotland, and the extent of the contrast may be represented in the following table:—

TABLE VII.—DEATH-RATE PER MILLION.
Under 1 year of Age.

		Males.								
Scotland		England and Wales		Northern Counties		Wales and Monmouth		Midland Counties		Southern Counties
105,741	...	86,329	...	103,177	...	91,990	...	77,349	...	72,441
Less than rate for Scotland	...	19,412	...	2,564	...	13,751	...	28,392	...	33,300
		Females.								
80,437	...	65,555	...	78,559	...	70,900	...	58,409	...	54,818
Less than rate for Scotland	...	14,882	...	1,878	...	9,537	...	22,028	...	25,619
		Ages 1 to 5—Males.								
16,242	...	11,711	...	15,391	...	10,522	...	9,414	...	9,968
Less than rate for Scotland	...	4,531	...	851	...	5,720	...	6,828	...	6,274
		Females.								
14,937	...	10,820	...	14,068	...	9,602	...	8,868	...	9,195
Less than rate for Scotland	...	4,117	...	869	...	5,335	...	6,069	...	5,742
Sum of differences	...	42,942	...	6,162	...	34,343	...	63,317	...	70,935

This difference in the death-rates under 5 represents an annual loss to Scotland at the rate of 43,000 per million living at these ages.

Deaths under 1 year of Age.

The death-rate per million living under 1 year of age in England and Wales is 86,239 for males, and 65,555 for females (say 86 and 66 per 1,000), and for Scotland 106 and 80. These rates for England correspond with the ratio of deaths to births; in Scotland, for some reason I have not yet ascertained, they are higher—the figures for Scotland for what is usually called the infant mortality rate would be 101 and 79.

Congenital Debility—Malformation—Premature Births, &c.

Figures representing the causes of death under 1 year are subject to many qualifications, and the following contrasts under this heading are submitted as strengthening the plea for unification of our methods of presenting the data of our national statistics. The figures can scarcely be accepted, I think, as indicating a biological variation in national vitality:—

TABLE VIII.—CONGENITAL DEBILITY—MALFORMATION—PREMATURE BIRTH, &c.

		Deaths under 1 year per Million living
SCOTLAND	...	43,061
ENGLAND AND WALES	...	35,062
Northern Counties	...	39,404
Wales and Monmouth	...	34,708
Southern Counties	...	30,498
Midland	...	33,969

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Infectious Diseases under 1 year.

The contrasts here and the excess in the Scottish rate are shown in Table IX, the numbering of the groups being similar to that adopted in Table VI for all ages:—

TABLE IX.—DEATH-RATES (UNDER 1) FROM CERTAIN INFECTIOUS DISEASES.
PER MILLION LIVING.

Groups of infectious diseases.	Males.					
	Scotland.	England and Wales.	Northern Counties	Wales and Monmouth	Southern Counties	Midland Counties
1 to 6 (a) ...	8,845	4,365	5,478	4,568	3,764	3,562
7 to 9 (b) ...	1,650	986	1,156	1,086	820	909
	<u>10,495</u>	<u>5,351</u>	<u>6,634</u>	<u>5,654</u>	<u>4,584</u>	<u>4,471</u>
10 to 11 (c) ...	2,473	1,610	1,963	1,405	1,388	1,445
	<u>12,968</u>	<u>6,961</u>	<u>8,597</u>	<u>7,059</u>	<u>5,972</u>	<u>5,916</u>
	Females.					
	Scotland.	England and Wales.	Northern Counties	Wales and Monmouth	Southern Counties	Midland Counties
1 to 6 ...	8,566	4,227	5,309	4,418	3,703	3,397
7 to 9 ...	1,253	723	898	667	664	597
	<u>9,819</u>	<u>4,950</u>	<u>6,202</u>	<u>5,085</u>	<u>4,367</u>	<u>3,994</u>
10 to 11 ...	1,903	1,245	1,444	954	1,147	1,170
	<u>11,722</u>	<u>6,195</u>	<u>7,646</u>	<u>6,039</u>	<u>5,514</u>	<u>5,164</u>

(a) Enteric fever, small-pox, measles, scarlet fever, whooping-cough, diphtheria.

(b) Influenza, encephalitis lethargica, meningococcal meningitis.

(c) Tuberculosis of the respiratory system and other tuberculous diseases.

Ages 1 to 5 years.

A similar analysis of the deaths from infectious diseases at ages 1 to 5 shows the following differences:—

TABLE X.—DEATH-RATES PER MILLION AT AGES 1 TO 5 YEARS.

Groups of infectious diseases.	Males.					
	Scotland	England and Wales	Northern Counties	Wales and Monmouth	Southern Counties	Midland Counties
1 to 6 ...	5,550	3,049	3,655	2,619	3,257 ²	2,336
7 to 9 ...	508	411	520 ¹	415	343	348 ¹
	<u>6,058</u>	<u>3,460</u>	<u>4,175</u>	<u>3,034</u>	<u>3,600</u>	<u>2,684</u>
10 to 11 ...	1,931	1,149	1,594	730	911 ³	965 ³
	<u>7,989</u>	<u>4,609</u>	<u>5,769</u>	<u>3,764</u>	<u>4,711</u>	<u>3,649</u>
	Females.					
	Scotland	England and Wales	Northern Counties	Wales and Monmouth	Southern Counties	Midland Counties
1 to 6 ...	5,829	3,250	3,917	2,865	3,359 ⁴	2,533
7 to 9 ...	429	349	487 ¹	300	272	325 ¹
	<u>6,258</u>	<u>3,599</u>	<u>4,354</u>	<u>3,165</u>	<u>3,631</u>	<u>2,858</u>
10 to 11 ...	1,505	983	1,311	675	826	827
	<u>7,763</u>	<u>4,582</u>	<u>5,665</u>	<u>3,840</u>	<u>4,457</u>	<u>3,685</u>
Excess deaths in Scotland per million living 1 to 5, compared with England and Wales					Males	
					Groups 1 to 6	2,501
					7 to 9	97
					10 to 11	782
						3,380
					Females	
					Groups 1 to 6	2,579
					7 to 9	80
					10 to 11	522
						3,181

¹ Influenza excess.

² Scarlet fever and diphtheria.

Other tuberculosis.

⁴ Measles and whooping-cough.

The Relationship between the Infant Death-rate and that of the Ages 1 to 5 years.

It has elsewhere¹ been suggested that conditions prejudicial to infant life continue to affect the immediately succeeding years, and there is evidence that a high infant death-rate is associated with a high rate during the 1 to 5 years period. This is shown in Table XI. But it does not seem to be the whole case, for if we view the

¹ "The House as a Contributory Factor in the Death-rate," *Proc. Roy. Soc. Med.*, 1913, vi (Sect. Epid.), pp. 155-190.

death-rate at these years as a percentage of the infant rate, the female ratio is always greater than that of males, although male infants are subject to a higher death-rate than female.

TABLE XI.—DEATH-RATE PER MILLION—ALL CAUSES.

	0 to 1		1 to 5	
	Males	Females	Males	Females
SCOTLAND	105,741	80,437	16,242	14,937
Northern Counties ...	103,177	78,599	15,391	14,068
Wales and Monmouth	91,990	70,900	10,522	9,602
ENGLAND AND WALES	86,392	65,555	11,711	10,820
Southern Counties ...	72,441	54,818	9,968	9,195
Midland	77,349	58,409	9,414	8,668

TABLE XII.—MORTALITY 1 TO 5 AS A PERCENTAGE OF INFANT MORTALITY.

	Males		Females	
	Infant mortality	1 to 5	Infant mortality	1 to 5
SCOTLAND	100	15.36	100	18.56
Northern Counties ...	100	14.91	100	17.89
Wales and Monmouth	100	11.43	100	13.54
ENGLAND AND WALES	100	13.55	100	16.50
Southern Counties ...	100	13.76	100	16.77
Midland	100	12.17	100	15.18

DISEASES OF THE ORGANS OF RESPIRATION.

We have already seen in Table VI that the rate for pulmonary phthisis is lower in Scotland than in the English divisions, excepting the Midlands. It might be said that as our rooms are larger, mass infection will be more diluted, but on the other hand it may be that a more rigid exclusion of the fibrotic chronic bronchitic from the chronic tuberculous lung may explain part of the difference. Be that as it may, the other causes of death from diseases of the respiratory organs present the same contrast as do the infectious diseases.

The following table shows, for all ages and for each sex, a slightly higher rate in Scotland for pneumonia, bronchitis and the other non-tuberculous affections of the respiratory organs. When tuberculosis of these organs is added, the male rate in England for all forms of respiratory disease exceeds that of Scotland, but not the female rate, so that, apart from tuberculosis, respiratory diseases would appear to be more prevalent in Scotland. Here, however, differences in method of classification must be kept in view. Diseases of the heart and lungs—less tuberculosis—taken together give an equal rate for both countries.

TABLE XIII.—DISEASES OF RESPIRATORY ORGANS. DEATH-RATES PER MILLION.

<i>Scotland :—</i>					Males	Females	Persons
18. Bronchitis	900	825	861
19. Pneumonia	1,291	929	1,103
20. Other respiratory diseases	213	165	188
					2,404	1,919	2,152
Tuberculosis of the respiratory system					865	773	817
					3,269	2,692	2,969
16. Heart disease	1,364	1,380	1,372
<i>England and Wales :—</i>							
18. Bronchitis	970	908	937
19. Pneumonia	1,145	777	953
20. Other respiratory disease	181	127	153
					2,296	1,812	2,043
Tuberculosis of the respiratory system					995	755	869
					3,291	2,567	2,912
16. Heart disease	1,442	1,532	1,480

TABLE XIV.
DEATH-RATE PER MILLION FROM CERTAIN DISEASES WHICH ARE NOT AIR-BORNE.

	Scotland			England and Wales			Northern Counties			Wales and Monmouth			Southern Counties			Midland Counties		
	M.	F.	P.	M.	F.	P.	M.	F.	P.	M.	F.	P.	M.	F.	P.	M.	F.	P.
13 Rheumatic fever	31	40	36	45	46	46	51	52	51	71	76	73	36	40	38	40	39	40
16 Heart disease ...	1,364	1,380	1,372	1,442	1,532	1,480	1,386	1,493	1,442	1,385	1,473	1,429	1,627	1,676	1,653	1,353	1,457	1,407
17 Arterio-sclerosis ..	166	120	142	442	288	367	504	319	408	311	199	255	475	347	406	379	253	314
25 Acute and chronic nephritis ...	423	351	385	358	297	326	383	334	358	376	356	366	375	297	333	312	246	277
24 Cirrhosis of liver	44	23	33	68	31	49	66	26	45	60	21	41	78	40	58	64	32	47
	2,028	1,914		2,355	2,204		2,380	2,224		2,203	2,125		2,591	2,400		2,148	2,027	
			1,908			2,268			2,304			2,164			2,488			2,085

M = Males; F = Females; P = Persons.

RHEUMATIC FEVER, HEART DISEASE, ARTERIO-SCLEROSIS, NEPHRITIS AND CIRRHOSIS OF LIVER.

In all these diseases, with the exception of nephritis, the rate for Scotland is below¹ each of the divisions of England and Wales, and the relationship is not altered by inclusion of the "other diseases of the circulation."

Two questions only need be suggested: (1) Is the nephritis rate in Scotland higher as a late result of our scarlet fever? (2) Is chronic alcoholism related to the higher rate in England from arterio-sclerosis and cirrhosis of the liver?

SUMMARY.

The foregoing illustrations are based on the deaths occurring in the years 1921-23. They do not exhaust the kind of information which a comparison of this sort brings out. They show a higher death-rate in Scotland for each sex at all ages, and also for children under 5, than occurs in any of the geographical divisions of England and Wales. To a considerable extent the higher death-rate among children arises from a greater prevalence of the infectious diseases of childhood, but especially of measles and whooping-cough. This excess is not special to the years under review, although measles shows a high death-rate in 1922. It would appear that since 1871, at least, whooping-cough has been uniformly more fatal than in England, and measles since 1891. The illustrations further show that for influenza and the infectious diseases of the central nervous system the death-rate for Scotland is again higher. The contrast presented between pulmonary tuberculosis and other forms of tuberculosis opens up a wide question regarding the relative prevalence of animal tuberculosis in the two countries.

Finally, the illustrations show that if we take another group of diseases altogether—one, so far as we know, not primarily related to the condition of the air supply—the contrast is entirely the other way, the rates, excepting that for nephritis, being higher in England. The obvious suggestion therefore is, I think, that without further inquiry we cannot dissociate the higher incidence of infectious diseases in Scotland from its system of housing in tenements.

Many years ago Sir Arthur Newsholme inquired into the vital statistics of the then comparatively recently erected blocks of tenement houses in London, as illustrated by the Peabody Buildings and others of a similar type, and compared them with those of London as a whole. Among the conclusions one reads:—

"The death-rate at different groups of ages is lower in the Peabody Buildings than for the whole of London, with the exception of the ages 0 to 5 and 15 to 25," and "... the diseases more immediately due to direct infection (scarlet fever, diphtheria, and, still more, whooping-cough and measles) ... are more fatal and therefore probably more prevalent."

Tenement houses differ much in design. But the common close, and the unventilated common stair, are in obvious contrast to the house which opens directly from the freely-moving external air.

Finally, there seems need for a much more exhaustive comparison of national death-rates than has been possible within the limits of this paper, and this implies a uniform method of classifying deaths.

Discussion.—Dr. JANET LANE-CLAYPON said that although she had been deeply interested in Dr. Chalmers' paper, she was not quite able to follow his hypothesis without some further investigation. She understood that Dr. Chalmers regarded the differences in the death-rates as attributable solely to housing conditions. Since Sir Arthur Newsholme's work on the Peabody Buildings had been published, a great number of large tenement dwellings had been built in London, and were to be found in boroughs such as Holborn, Chelsea, Westminster, and so forth—districts in which the mortality rates were very favourable. She was not sure of the precise meaning attributed by Dr. Chalmers to the term "cottage." Did he regard as cottages the immense number of so-called "let-down" houses which formed the dwellings for working-class people over what must amount in all to

¹ When the sexes are taken separately certain differences are seen. Males in the Midlands have a lower rate in group 16; and in Wales and Monmouth the female rate for group 25 is higher and in 24 lower.

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some square miles scattered over the northern parts of London? These houses were certainly not cottages in the ordinary acceptance of the term, and she thought that the staircases, which were often in a poor state of repair and not always by any means well-ventilated, were not so satisfactory as the staircases in the majority of the tenements. It would, she thought, be possible to obtain sufficient data of mortality-rates from the tenement dwellings in London to compare with those of Glasgow. However, as Dr. Chalmers had said, there were "tenements and tenements," and it might well be that the tenements of London would not be suitable for such a comparison with those in Glasgow.

The PRESIDENT, Dr. GREENWOOD, Dr. TAPPER, and other Members of the Section took part in the discussion.

Dr. CHALMERS (in reply) observed that there was nothing in the analysis to suggest that tenement life might not be as healthy for adults as life in hotels or barracks; but the position was different for children under 5 years of age, especially with regard to infectious diseases. As affecting them the conditions were more comparable with what occurred in a residential school when invaded by measles, except that the child population of the tenement was younger and more susceptible to fatal attack. With regard to the general death-rate for the Northern Counties, which most nearly approached that of Scotland, this was caused not by infectious diseases at ages under 5; in these counties males had a higher death-rate from 5 years onwards and females at selected periods (5 to 15 years) and from 65 years upwards. But the higher rates in males were due to pulmonary tuberculosis, bronchitis and pneumonia, rheumatic fever, heart disease, arterio-sclerosis, diabetes, &c., which for the most part were outside the category of air-borne diseases.

With regard to uniformity in classifying the causes of death, it was, of course, quite true that no method of recording could be more accurate than the prevailing custom in certifying them. It might be difficult to arrive at an international system, but, as between the populations north and south of the Tweed, it did seem worth while making an effort at a greater uniformity than was at present illustrated by the contrasts presented in the classification of diseases of the heart and lungs.

POSTSCRIPT.—Arising from the suggestion of Dr. Major Greenwood, I have taken occasion since the discussion to compare the death-rates of Manchester and Glasgow for the years 1914-1922.

Excluding measles from both, the average rate for Glasgow was 16.1, and for Manchester 14.3, a difference of 12.6 per cent. in favour of Manchester. But the measles death-rate of Glasgow for these years exceeded the corresponding rate for Manchester by 69 per cent. If we exclude 1922, when the rate for Glasgow was unusually high—being two and a half times that for Manchester—the excess for the others years was still 51 per cent.

[January 22, 1926.]

The Influence of the Universities upon the Advancement of the Public Health.

By Professor E. W. HOPE, O.B.E., M.D., D.Sc.

It is easy to-day to appreciate the influences and the value of the co-operation of the Universities in the advancement of the public health: research in the laboratory and in the field; the training of administrative officers of all grades; whose duty it is to apply the ever-increasing knowledge the demonstration to governing bodies of the fact that money properly spent in lessening the sum of avoidable human miseries is worth spending, advancement of an educated public opinion in those matters; and the making plain to every citizen what lies in his power to do for himself. But we must remember that the more successful are sanitary operations, the less apparent is the need for them. Memories are short, and if we make a clean sweep of our historic past, so far as the prevention of disease is concerned, and fail to keep alive the recollection of bygone conditions, we lose the lesson which experience has taught, as well as the full significance of the initiation of the movements from which so much resulted.

The share of the Universities in the advancement of public health is one of the many interesting features of this important subject. Until comparatively recent times, it does not appear that the Universities, as such, took any interest in the matter, nor were they in a position to give help of any kind to those who were endeavouring to lessen the mass of preventable human misery directly associated with preventable disease and mortality. If we look back to the recorded circumstances of our towns, about the middle of the nineteenth century—a short period in their history—we find that in almost all of them there were thoughtful men and women, some of them in responsible social positions, gravely exercised by the condition of things; some one or two, most usually a doctor, occasionally a clergyman, or a philanthropist or engineer, were prompted in times of special epidemic visitation to give expression to what they believed to be some possible remediable policy, and Edwin Chadwick's writings were already, in a measure, pointing the way for them. Furthermore, there were a few individuals within the Universities who gave strong expression to the view that the grave social problems of the masses of the people called for their attention. The evils exposed by these means did undoubtedly attract public attention and did lead to the adoption of certain measures, some of which were ameliorative and helpful, but others, owing to haphazard direction, were followed by opposite consequences; for example, at the commencement of the great cholera outbreak in Exeter, the feeling that the freer use of water was desirable led to the reopening, with disastrous results, of many shallow wells which had been closed on account of their obvious pollution by faecal filth.

Various reports, in the early part of the Victorian era—more especially those of Royal Commissions, and notably one in 1840 appointed “to inquire into the circumstances affecting the health of inhabitants of large towns and populous districts, with a view to sanitary regulations”—revealed evils of a magnitude wholly unknown to those responsible for the government of those towns, and the shock to public sentiment occasioned by these reports also awakened an interest within the Universities. These reports in the main were limited to two arresting circumstances; first, the extraordinary prevalence of disease and destruction of life, and secondly, the gross structural defects with which they were associated, notably in regard to dwellings, the construction of alleys and cellar-dwellings, the absence of sewerage and the complete neglect of scavenging. Graphic accounts are given of the condition of many of the great urban centres, Leeds, Manchester, Liverpool, Bradford, Hull, Coventry, Glasgow, and others, as well as of the many individual townships which, aggregated together, constituted London. One town is singled out as being better than the rest, viz., Birmingham. Birmingham, the Committee say, inhabited by so many industrial mechanics, so long celebrated for their skill and ingenuity, appears to form a rather striking contrast with the state of other large towns. This is attributed to the better pay and more constant employment than what prevails in other towns.

Dr. Neil Arnott was among the first to express the view that by proper sanitary police regulations the condition of London might be improved, and the remedial measures would *cost less* than it cost at that time to provide for the sick, the widows and the orphans. Southwood Smith summed up the position, so far as defective sewerage and scavenging go in the poorer parts of twenty metropolitan unions, by the statement “That it is utterly impossible to convey to the mind an adequate conception of the filthy and poisonous condition in which large portions of all these districts constantly remain,” and he remarks that *if* it should be found that similar conditions exist in all large towns in Great Britain, there would seem to be a proper and legitimate field for the exercise of legislative wisdom and power.

An effective argument to show that all classes of the community of London were directly interested in the subject was put forward by Dr. Farr, when he pointed out that although the epidemics arise in the east end they do not stay there—they drift

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to the west end, and prove fatal even to well-to-do dwellers in wide streets and squares.

Birmingham held the best position amongst the towns. Liverpool could lay no claim as a rival. In his well-known report on the sanitary condition of the labouring population of Great Britain, Sir Edwin Chadwick deals with Liverpool. Dr. Duncan, a physician practising in Liverpool, in his evidence before the Royal Commission of 1840, stated that 38,000 persons were living in cellars, the construction of which was primitive, mostly having the bare earth for a floor, although straw was provided. The charge was one penny a night, and the numbers of both sexes occupying the place were usually too great to allow the doctor to enter without stepping on, or shifting some of them; in the centre of the cellar a hole was dug which was used for all purposes, in the absence of any other drainage or sewerage. Courts and alleys, of which he gives full descriptions, were wholly without drainage, and scavenging was completely neglected. Some 86,000 persons were housed under these conditions. The reason assigned by the witness for the occasional absence of typhus from certain specified areas was that all the inhabitants had already had it. The want of adequate water supply aggravated every evil.

"Liverpool is the second port of the Kingdom?" the witness was asked. "I believe it is," was the answer. "Do you observe a great deal of discontent among the poorer people?" "No, they seem quite contented in whatever condition they may be."

What the inducements may have been to send their children to school becomes obscure when we read that the common day schools, to which a very large number of the poorer children resorted, are described by another witness, Mr. J. R. Wood, as wretched in the extreme, corresponding in a remarkable degree with the condition of the people—dark, damp and dirty garrets were used as school-room, dwelling and dormitory; more than forty of them were cellars. The atmosphere was so offensive as to be intolerable to a person entering from the open air, a condition aggravated by filthy and offensive odours from other causes. The "dame schools" where reading, sewing and knitting were taught, were very similar.

Although not a medical man, this witness evidently was an observer; he remarked that measles, scarlet fever, small-pox and ophthalmic affections never attack one scholar alone, frequently half of the scholars are affected at the same time, and some schools have been visited when two-thirds of the children usually attending were detained at home by such complaints. The witness expressed the belief that diseases acquired greater virulence in the case of these schools. It is not surprising that the appearance of the children was described as dirty, squalid and depressed, yet many appeared quite healthy. The dimensions of one garret, approached by three pairs of dirty, broken stairs, and occupied by thirty children, was 10 ft. by 9 ft. Dogs, cats, or even poultry were met with in those school-rooms.

The Royal Commission had no difficulty in coming to very definite recommendations as to environmental improvement, and voiced the necessity for legislative powers, without which it would be utterly impossible to make a beginning. But the legislative assemblies, unhappily, were uninformed—ignorance is the mother of contention. Parliamentary committees did not connect in their own minds the conditions described with the prevalence of disease; vested interests were strong, cost was high, land was dear, water supply difficult of provision; the outlook of municipal rulers was almost restricted to sewers and sewage, whilst one town was applying for powers to compel house-owners to connect their drains with the public sewers, another was seeking powers to prohibit such a procedure. Parliament granted both requests, on the grounds, in the second case, that a refusal would lead to public cost if additional or larger public sewers were provided.

The report of this Commission had much effect upon educated public opinion outside the Universities, but apparently failed wholly to stimulate action within

them; it certainly led to some enlightenment of the public in the great provincial centres, and this was followed by a great deal of local legislation, designed to facilitate ameliorative measures. Two years later, in 1842, Dr. Duncan was appointed in Liverpool to advise on health matters, and was the first medical officer of health to be appointed in this country. A year later Sir John Simon was appointed to a similar post in the City of London—offices purely advisory, however, since they had neither parliamentary powers nor staff.

One point which influenced general public opinion, perhaps more than anything else, was the gradual realization that a great saving of cost and a great reduction of the poor rates would ensue from an improvement in the condition of the people. That public opinion had been aroused is shown by the fact that in 1844 Commissioners were appointed to inquire and report further on the state of the large towns and populous districts. It is interesting to note the activity in regard to legislation resulting from the confirmation of the fact that the responsible authorities appear to have been unaware of the real state of things, which was fully established by the returns in the registers of deaths. The Commissioners, further, dwelt upon the lively and cordial interest taken by the inhabitants in these matters, and the ready assistance afforded by persons of every class and denomination.

Meanwhile constant additions to the *local* legislation that Parliament had granted were found necessary, and it may be mentioned that this *local* legislation, obtained by provincial centres, ultimately formed the basis for the Public Health Act of 1875.

As a result of local effort, based upon local legislation, considerable improvement had been reached by 1860-70; more people were becoming interested, the removal of the grosser evils had brought into prominence others, less arresting but not less harmful. The recognition by thoughtful people, both within and without the Universities, that efforts were squandered from misdirection, was not helpful, because at that time it merely led to the mischief associated with destructive criticism. The corporations found their task a hard one, the money expended on the half-measures adopted had not achieved the expected results, their efforts were regarded as manifest failures, they were discredited and discouraged and felt that they were fumbling along the wrong path. If, as appears to be the case, the Universities offered no help in these early struggles, the reason is plain; they were not in a position to do so, they had never considered the matter, and experience and knowledge were wanting. In 1860 one of the northern centres—Liverpool—whose difficulties were greater than the rest, sought advice from an outstanding scientist of the day, Professor Huxley, upon whose advice the first direct appeal to a University was made. Burdon Sanderson (of Oxford) and Parkes, the military hygienist, ultimately presented a most valuable report, which, whilst dealing mainly with structural conditions, sewerage and refuse-disposal, made general allusion to individual habits and conditions.

"Drunkenness and the consequent poverty, degradation and squalor, led," as the report states, "to starvation and beggary. The children are in rags and filth, and the unhappy people seem to know none of the comforts, and few of the decencies of life, and widespread habits of drunkenness, and consequent want of food, aid their wretched homes in destroying their health."

As we shall presently see, it was during the decade 1860-70 that interest in this aspect of social welfare was growing within the Universities, not unstimulated by severe visitations of the University towns themselves by cholera in preceding years.

Whilst nearly all the large centres had similar problems, reference is made in the report to one peculiar to Liverpool, which explains its additional difficulties and which is of special interest to epidemiologists. It is, moreover, the forecast of port and international hygiene, which has been so remarkably developed in recent years. The following is the statement:—

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"The introduction of typhus, cholera, small-pox or relapsing fever is always attended with epidemic outbreaks, if the disease prevail in places with which it is in frequent communication as a seaport. It is not possible," they say, "to alter this without surrendering the commercial supremacy of Liverpool (!) but some precautionary measures may be taken."

Efforts, they suggest, should be made to obtain regular monthly reports of the health of foreign countries as regards epidemic diseases, so as to be prepared for any contingency of the kind.

It was in the same period that Sir Henry Acland, Regius Professor of Medicine at Oxford, had begun to take an active interest in hygiene, and it would seem largely owing to him that another Royal Commission had been appointed to inquire into the unsatisfactory condition of metropolitan and other drainage. William Stokes, Regius Professor of Medicine at Dublin, and Acland were fast friends; Stokes was one of the earliest, ablest and most distinguished advocates of the doctrines of State Medicine, and for many years used all his powers of mind, of eloquence and of learning to advance those doctrines. It was to him that the initiation of the teaching of the subject in Dublin University and the founding in 1872 of a diploma in State Medicine in connexion with Trinity College, were mainly due. At the first examination there, in 1876, there were four candidates, the sole survivor of those four being Sir John Moore, to whom I am indebted for much information on these points. Stokes' hopes for the future of the work he was fostering may be gathered from an address which he gave at the University of Dublin in, I think, 1872, from which I will quote a paragraph, not only because it reflects the conditions and the feeling of the time, but also because so much of his pre-vision has been realized.

"A time *may* come," he says, "when the conqueror of disease will be more honoured than the victor in a hundred fights. The time *may* come when no man for his own ends or for his own profit will be permitted to damage the health or the well-being of his neighbour or of his servant, or his employee, nor the prisoner have to suffer through the ignorance or the indifference of his jailer, while the emigrant with his loved ones will be protected from disease as he expatriates himself from the land of his birth."

"The gifts to man from Heaven—pure air, pure water, bright light and wholesome food—will be more freely shared in, and the moral and physical evils of overcrowding and the consequent guilt, the shame and the pestilence, will disappear."

In the case of the University of Edinburgh the sequence of events had been somewhat different; certain aspects of the subject had been systematically dealt with at the medical schools in Edinburgh earlier and to a fuller extent than in any of the other Universities. The sequence of the teaching of the subject affords an interesting explanation of the association of the prevention of disease as a science with the science of Medical Jurisprudence. These subjects, to-day, are really as wide apart as the poles, but at that time many of the problems with which each was concerned had a common origin. Public health, as a science, crept into the Universities in the tracks of the medical jurist simply because conditions favouring spread of disease were identical with those favouring the crimes of violence which, at that time, furnished the main claims upon the attention of the medical jurist. Public health problems, under the title of "Medical Policy," were included in Professor Traill's lectures at Edinburgh, under various headings, before 1862, for instance, prostitution, sewers, schools, effects of dwellings on health, climate, &c. His syllabus would appear to have been founded on French and German text-books of that day. "Medical policy" was considerably amplified by Sir Douglas Maclagan, but perhaps received its greatest stimulus and most practical application from Sir Henry Littlejohn, who was lecturing on the subject at the extra-mural school of medicine long before his appointment to the Chair of Medical Jurisprudence within the University. He was at that time Medical Officer of Health of the city, and he availed himself of the very exceptional opportunities which that position gave him in connexion with practical instruction. A diploma course had

been instituted in Edinburgh in the early seventies, and a B.Sc. degree was established in the University shortly afterwards, in the subject of Public Health. It seems fitting, therefore, that it should have been at the University of Edinburgh that a philanthropist was to endow the first "whole-time" professorial chair of public health in the Kingdom; this was in 1898. The chair is now held by Professor Lelean.

At the University of Glasgow Sir William Gairdner had been appointed to the Chair of Medicine in 1862, and he was, for ten years following, the chief Medical Officer of Health of Glasgow; he not only had a large share in laying the foundations for the public health system of that city, but provided facilities for the teaching of public health methods and administration. Further developments of the subject which ensued are due to Professor Glaister, whose chair, really one of Forensic Medicine, largely favoured the promising hand-maiden, Public Health. A separate lectureship in public health, subsequently held for a time by Professor Allison, suggested a parting of the ways in regard to the teaching of public health as a separate subject apart from medical jurisprudence, and the foundation in the University of Glasgow of a special Chair of Public Health in 1923, to which Professor Currie was appointed, is a fitting recognition of the importance attached to it. The Universities of Scotland are not the only ones with endowed whole-time chairs; at the University of Cardiff the Talbot Chair of Preventive Medicine was founded in 1915, to which Dr. Collis was appointed. London will, I presume, be in a similar happy position within a short while.

Once the subject had obtained a foothold, the Universities of Oxford and Cambridge were not slow to recognize that the health and well-being of the people were subjects not outside the scope of their attention, but it is clear that among the many difficulties which obstructed advance was the fact that the most appropriate lines of research and teaching had still to be found. Under the Public Health Act of 1872, every Sanitary Authority was required to appoint a Medical Officer of Health; this Act gave a powerful stimulus to the foundation of courses of systematic instruction, and in due time diplomas for special knowledge of the subject were granted—Dublin in 1872, Cambridge, largely under the stimulation of Dr. Liveing, in 1874, and Edinburgh at about the same time. At the University of Cambridge the subject was fostered under the influence of Mr. Purvis, the late Sir Sims Woodhead, and others; the course of instruction largely attended, and the diploma in Public Health, given under the State Medicine Syndicate, was a popular one, and its high standard has been fully recognized by administrative bodies. The University of London, in 1875, instituted an examination in subjects which related to public health, and awarded a certificate of proficiency in these subjects. This examination, as in the case of the other Universities, was only open to Bachelors of Medicine. The first examination was held in 1876, the same year apparently as the first examination at Dublin; it is interesting to note that the examiners were Dr. Farr, Dr. Fraser, Captain Douglas Galton, and Sir John Simon. There was one successful candidate, our late and much esteemed friend, Dr. Henry Franklin Parsons. At the University of London, as elsewhere, the syllabus has been varied and improved as time went on, and the scope of examination enlarged, the syllabus of the early days being far removed from that with which we are now familiar. The subject, however, never seemed to be popular with candidates, who were few until 1887, when interest was revived. In this year there was a record number of successful candidates, which, however, only reached a total of three; the first amongst them, and the gold medallist, being Sir William Collins. In the preceding year, 1886, the General Medical Council had taken action and Public Health diplomas became registrable under the Medical Act. In 1887 the movement was set on foot by the General Medical Council to standardize the qualifications issued by the various Universities. In June, 1888,

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public health was recognized in the University of London as a distinct branch of study and subject for examination, and the Senate established a degree in State Medicine in place of the certificate in Public Health, to be awarded to Bachelors of Medicine. The Local Government Act of 1888 required that a medical officer of health appointed after 1902 should be the registered holder of a diploma in public health.

When the University Colleges of Manchester, Liverpool, Leeds, Cardiff, Sheffield, and Birmingham, raised themselves to University dignity—and for our present point of view I may include Durham—the importance of the subject of the health of the people had received full recognition; professorial chairs or lectureships were very soon established, and courses of instruction instituted and developed in all of these Universities as opportunity arose. Provision was made for the training of medical officers of health and their ancillary staff, medical officers of schools, of welfare clinics, of tuberculosis and V.D. clinics, and so forth. Similar provision was also made for city and county bacteriologists and analysts, and in some instances for the education of the general public.

Whilst the necessity for the training of the higher, professional, or expert administrators is now unchallenged, the equal necessity with regard to the training of the rank and file of the sanitary army is not yet so fully recognized. Knowledge which is the possession of a few can only benefit a few. Just as in the monastic days of the older Universities the value of the trained itinerant preachers was recognized, so to-day the Universities, or some of them, recognize the vital importance of the training of those officers who are in daily touch with the people, and whose business it is to translate and apply established facts. Amongst this class are sanitary inspectors and health visitors, the staffs engaged in the inspection of meat and foodstuffs, or in the suppression of smoke and the proper control of boiler furnaces, and so forth. It is in connexion with the University Schools of Social Science, or Public Health, that this training is provided, and the certification of the candidate follows, as in the case of the diploma for the medical officer. Generous grants towards the cost of this training are made by the Ministry of Health.

It is clear that the policy of present-day health movements is increasingly directed to educational methods. It is with these objects that sanitary inspectors, welfare workers or health visitors are employed, that clinics are established and that industrial employers safeguard their employees. "Health Weeks," "Baby Weeks," lectures, literature, models, exhibitions, all help to create an educated public opinion, and we all of us appreciate the services of the statesman, distinguished cleric, or popular actor, or actress who is good enough, on occasion, to convey to the public the homely truths, which are so much more arresting when coming through these channels rather than through the usual ones.

In conclusion, I would express the view that while there is no need to fear that the Universities are likely to slacken in their interest, one need only study the writings of Simon, or J. B. Russell, or many others, to find, as one might expect, that the influences of the Government, to encourage or discourage, are very potent. I am aware that some of my friends at the Ministry dissent from many of the views which I have expressed in regard to the training and certification of sanitary staffs, and I am also aware that such views are apt to be passed on unquestioned to still higher officers, gathering force as they go. We find expression given to the view that Universities, however good the provision may be for the teaching and training of these officers, and at whatever cost of money or time that teaching is provided, should no longer be regarded as fit bodies to certify the competency of their alumni to carry on their duties. The view is voiced that a body which has never concerned itself with the training, and indeed is wholly new to the work, should replace the Universities. Whatever sympathy one may have with the desire to transfer these important duties to a central body in London, a preliminary conference with the

Universities interested, which have done so much to advance the public health in every direction, would have had the advantage of affording an opportunity for the interchange of views, which is at all times valuable. In this case, as in others, I have not the least doubt that, as all are aiming at the same thing, the public health will gain in the end.

Discussion.—Sir GEORGE BUCHANAN drew attention to the value of the historical method of considering this subject. If Liverpool was taken as an example, the contrast between the present conditions of public health administration and education with those of thirty years ago was striking. Dr. Hope had himself taken a share in bringing about these developments, for which British hygiene was lastingly in his debt. He (Sir George Buchanan) trusted that we were consolidating in this country the relations between our practical hygienists and our Universities. They needed to be closer. The contrast was always noticed at international conferences when expert committees were appointed. All other countries at once, and naturally, nominated as their public health representatives those who were professors in their medical schools or institutes; with us that was rarely the case.

Sir George Buchanan also added some observations on the advantages of the "one portal" of entry into public health work, and of the danger of over-specializing and of officially requiring qualifying examinations in limited branches of the subject. The degree or diploma in public health should testify to a wide outlook and the possession of basic knowledge of all branches of the work. Specialization for administration in tuberculosis, school inspection, child welfare and other subjects could then be entrusted to the holder of the degree or diploma, to obtain by experience.

Major-General Sir W. MACPHERSON said he would like to make one observation on Professor Hope's paper, to which he had listened with great interest. He understood Professor Hope to say that the first whole-time professorship of public health was at Edinburgh University. But, if you grant the status of a medical school to the Army Medical School, it was in it that the first whole-time professor of hygiene was appointed in the person of Professor Edmund Parkes. Indeed, Professor Parkes was the pioneer in teaching hygiene, which he commenced in the newly instituted Army Medical School after the Crimean War; and his "Manual of Hygiene," published first in 1865, was the first comprehensive work on the subject. In fact it was this influence that induced the other teaching schools and Universities to include hygiene in their curriculum and appoint professors to teach it; so that the credit of the first professorship of the subject must be given to the Army Medical School.

Dr. G. CLARK TROTTER (Medical Officer of Health of Islington) drew attention to a point in connexion with the rôle of the Universities in education in hygiene and public health which really had been covered by the interesting paper by Professor Hope, although the author of the paper, in his modesty, had not laid emphasis upon it. He referred to the close relationship of the Professorial Chair to the office of Medical Officer of Health in several of the Universities. Quite recently the University of Edinburgh had associated the Medical Officer of Health of the city with their teaching, and at one time Sir Henry Littlejohn, the Medical Officer of Health, lectured on the combined subjects of Medical Jurisprudence and Public Health. In the University of Aberdeen, Professor Matthew Hay, Medical Officer of Health, held a similar double position, and it must be known to many, personally, that the excellent teaching which had existed in Liverpool was due to the close association with the public health work of the city. It was indeed a great asset when the University students were able to get, through the official position of their professor or lecturer, the "run" of a public health department, and the front seats in the local court when important cases were being tried.

As regards the general education of the student in public health, especially when he specialized in the subject, it should be borne in mind that the best experience was derived from the facilities for practical work; for instance, the future medical officer of health should not be entirely without any knowledge of the conditions of general practice, and it was a wise thing to gain for a period such a knowledge as an assistant. In the same way he was expected by the general practitioner to have a wide knowledge of infectious diseases. This could not really be gained by a short course, or even by two short courses taken at an infectious diseases hospital. It was a decided advantage to gain such experience as a resident medical officer. Professor Hope had shown, both in his historical review and in the instances he had

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cited, that the great teachers in hygiene had had a broad outlook, the result of wide experience. He was sure they had all gathered much from the paper of Professor Hope, who had such wide practical experience of the combined post of Professor and Medical Officer of Health.

Dr. GOODALL and Dr. GREENWOOD also took part in the discussion.

Professor HOPE (in reply), expressed his firm belief in the realization of the desire expressed by Sir George Buchanan for the increasing closeness of the relationship between the administrative and the educational sides. The international aspects of hygiene, to which Sir George alluded, were of supreme importance, and the advantages which had resulted from the various international conferences were so great that they served as an incentive to still closer international adjustments. So far as degrees and diplomas in public health were concerned there was little, if any, doubt that those who possessed them had undergone a very full training.

Sir William Macpherson's reference to the work of Professor Parkes, and his occupation of the Professorial Chair at Netley, furnished a ready explanation of his association at Liverpool with Professor Burdon Sanderson. The well known "Manual of Hygiene" certainly had proved a most valuable work in connexion with the subject of public health, as well as of military hygiene.

Dr. Trotter's observations, as well as those of the President and other speakers, emphasized the importance of the close association of the University work with the practical and administrative work in the cities and the great centres of population. The modern trend was to associate the professorial chair with this practical teaching, either by combining the two offices of lecturer and medical officer of health, or by closely linking the two departments together in some other way, as was now done in Edinburgh.

It was felt that the training of the subordinate officers, both male and female, was of great and increasing consequence, and every inducement should be held out to the Universities to make provision for the training of this important section of the staff of a health department. This had been done very fully in the University of Liverpool, probably because of the close association of University and City, and also on account of the very great sanitary necessities of Liverpool, to which, including the exceptionally complex problems of civic sanitation, were added those associated with the many interests, both in regard to health and commerce, of a great seaport.

Educational influences would be still more effective when the Universities were able to add to their teaching staff a lecturer whose special duty it would be to give explanatory public addresses at the various civic centres provided for social and educational gatherings.

Section of Epidemiology and State Medicine.

President—Dr. JOHN C. McVAIL.

Experimental Epidemiology : Some General Considerations.

By M. GREENWOOD and W. W. C. TOPLEY.

SIX years ago Dr. F. G. Crookshank contributed an interesting paper to the proceedings of this Section, entitled "First Principles: and Epidemiology." Dr. Crookshank was not very favourably impressed by the general level of epidemiology and remarked with truth that "few indeed of those who sit in offices and peruse records, tables and other statistical paraphernalia are gifted with the scientific imagination that enables them to form a picture of *all* that is passing beneath the eyes of others who are at work in general practice, in the dispensaries and in the casualty departments of our vast metropolis." He also said that "field work is required now more than ever, it is true; but it is also no less true than when Darwin said so, that, without hypothesis, there is no useful observation." We unreservedly accept these statements, the truth of which our several avocations have given many opportunities to realize. The statistician is the last person who needs to be told that statistics hardly ever tell one the whole truth and never tell one anything worth saying, unless one knows what question to ask. The bacteriologist does not want to be reminded how unilluminating can be the results of field work carried out with unimpeachable technical skill and without imagination.

We are not sure that we agree with Dr. Crookshank either in his explicit opinion that the "free discussion of fundamental and general principles will lead to better and more fruitful work, by those who have chosen certain lines of research for their own," or in his implication that an attentive study of, say, Ballonius, would help us to mend our ways. But we have certainly no pretension to lay down the epidemiological law to others. We hold merely that why *we*, and people like ourselves, do not understand the epidemiology of any disease (if for brevity we may still be permitted to use that unphilosophical word) is because we simply do not know enough to understand the answers which "Nature" is giving every day to our rather unintelligent questions. We are in fact, like Macaulay's imaginary Frenchman who, knowing just English enough to read *The Spectator* (with a dictionary), should attempt to defend the authenticity of Ireland's *Vortigern* and *Rowena* against Malone. That Frenchman would not have done better by embarking still more deeply upon textual criticism; he should return to his grammar and dictionary. It has seemed to us that before we could hope to understand "epidemic constitutions" and suchlike high matters, before we could even explain how scarlet fever epidemics arise—a matter still, it would seem, just a little uncertain—it might be well to practise on epidemiological events more within our control or, shall we say, less wholly beyond our control. It was that motive which led us to enter into a scientific partnership some years ago. The articles of association were these. That we should each bring into the common stock such special knowledge of particular techniques as we had individually acquired, but that the business of the firm should really be a joint one, that neither partner was at liberty to disclaim not mere formal but real responsibility for the work of the other.

We have worked together on this basis for some time and the object of this paper

¹ *Proceedings*. 1920, xiii (Sect. Epid.) pp. 159-184.

is to enlist the sympathy of those who are concerned with larger problems of epidemiology. We sail some of our model yachts in the children's pond and invite real sailors to tell us whether their motions have any instructive resemblance to those of real ships. Simple as are our conditions in comparison with those of real life, for we are wholly concerned with populations subjected to a quarantine of much greater rigour than the most autocratic sanitary authority has ever been able to enforce and exposed to infections qualitatively restricted, they are not absolutely simple and have given rise to various complex problems of interpretation. We shall, therefore, confine ourselves to the discussion of only a few problems, taking results which, as we think, have the most immediate relevance to the problems with which practical epidemiologists have to deal.

We take first the question of persistence. We think it is correct to say that just as the old prescription of flight into clean air was motivated by, or at least rationalized into, a doctrine that epidemic illness was "caused" by a noxious condition of the "atmosphere," the modern prescription of isolation hospitals made its appeal to the belief that the best way to stop infectious epidemics was to shut up affected persons. The shutting up of persons suffering from, for instance, scarlet fever, has been going on for two generations. In London only a very small proportion of the ostensibly affected escape segregation. Neither statistics, however, nor general medical opinion, give the least indication that scarlet fever is at all less prevalent than it ever was. Why this disappointing result should be found is a question different epidemiologists have answered in different ways. One answer is that scarlet fever is now so mild that many more cases are missed and there is more uncontrolled infection. The mildness of present day scarlet fever can, however, hardly be attributed to isolation, since even in the short period of 250 years the malignancy of scarlet fever has undergone at least three revolutions. A century ago it was very mild, fifty years ago it was very malignant.

We must of course keep these two properties, malignancy and prevalence, distinct in our minds; for the moment let us consider prevalence. In the course of an official inquiry now almost completed, one of us and his official colleagues have had to examine the whole of the evidence respecting the prevalence of scarlet fever in this country, to attempt to answer the question: Does hospital isolation have any effect upon the *incidence* of scarlet fever? Officially there are really only two ways of trying to answer that question. The first is the directly statistical. We can use the figures of isolation rates, notification rates, and such other indices—say overcrowding rates—as we may think possibly relevant, and measure the relation between isolation and notification rates by some technical method of statistics. The second method, the indirectly statistical method, is to ask a number of persons with administrative experience of scarlet fever whether they think isolation has affected incidence. Both methods have been employed and have led to the same conclusion. All applications of the calculus of correlations have wholly failed to bring out any connexion whatever between the incidence rate of scarlet fever and the extent of isolation. The variables are independent, for all practical purposes. The other method gave this result: Of 726 medical officers of health only a few more than half (369), believed that isolation favourably affected incidence. The interpretation of these indirect statistics is, of course, affected by psychological conditions. But even medical officers of health are human. If in a plébiscite of cobblers only a bare majority could be obtained to favour the proposition that boots keep the feet dry, one would surely have more than a doubt as to the economy of re-soling. It would be interesting to apply these two methods to a still more drastic case, that of the diseases of animals other than man. It is true that in some parts of the country the isolation of scarlet fever patients is so complete that few escape removal. In London in 1923, 13 Metropolitan boroughs isolated 95 per cent. or more of the notified cases. But segregation in a comfortable hospital for a few weeks is a much

less radical application of the principle than the immediate slaughter of affected members of the community. Our veterinary colleagues used to apply this principle in all its rigour to swine fever, and still apply it to foot-and-mouth disease. Neither disease seems to have been eliminated, but the data open to us are too scanty to merit discussion. We can certainly say that foot-and-mouth disease behaves precisely as we should have expected it to behave by analogy with our experiment—shortly to be described—if certain conditions are fulfilled, but we are not in a position to say that those conditions *are* fulfilled. Returning, then, to the case of scarlet fever and assuming that segregation has in fact failed to diminish the prevalence of the disease, we must seek an explanation. That which suggests itself at once is the phenomenon invoked by several epidemiologists and utilized with particular skill by Sir William Hamer to account for the periodicity of measles, viz., the introduction into the community of susceptible individuals. Is it possible that we can maintain an infectious disease indefinitely by adding to a community unaffected individuals? To this question we have sought a decisive answer. The experimental procedure has been this: We started with an acute infectious disease of bacterial origin, a pasteurellosis, which had occurred spontaneously among a batch of purchased mice, but which has never spontaneously occurred in normal stock. The original herd consisted of animals some of or all of which had survived exposure to the infection. The herd was housed under conditions which would make the mouth of the most autocratic and scientific medical officer of health water. There was no question of mere spraying the walls and whitewashing the ceilings after the removal of a case. Every day, whether a case of disease occurred or not, the whole population was transferred to fresh sterilized habitations and all their furniture was sterilized. There were no fomites, and the housing conditions were ideal. Certainly the gregarious and combative habits of the mouse did lead to overcrowding—the practice of living in the kitchen and having a museum is carried to excess by mice—but the potential floor space was on a princely scale.

Immigrants to the community were supervised far more jealously than on Ellis Island. They were housed in cages similar to those of the herd, in groups of five to eight for three weeks. If any died during that time and autopsy revealed an infection known to cause epidemic disease, all the candidates for immigration were at once killed. If a death occurred for which no cause could be found, the quarantine period was extended by 14 days, and if a second death occurred the survivors were sacrificed. This process, so far as pasteurella was concerned, was completely successful, but *Bacillus aertrycke* and *Bacillus gaertner* sometimes got through the barrage and complicated the experiment.

The herd was recruited only by immigration; any young not devoured by the adults were removed.

The experiment to which we wish to direct attention first has been going on for nearly five years, which is, taking into consideration the relative lengths of life of mice and men, equivalent to much more than a century of human history. The Pilgrim Fathers of the community were 26 mice, survivors of a previous experiment, who founded the new colony on March 5, 1921. For a little more than two years until April 30, 1923, three approved immigrants were admitted daily. Since then only one immigrant has been admitted daily.

The history of this little community, wholly exempt from *res angusta domi* in any sense of the phrase, well fed, well housed, with nothing to do but eat, fight, make love and sleep, shielded from contamination by super-medical officers of health, and most efficient birth control, is interesting in many ways. Let us first consider it from the standpoint of the non-medical historian, i.e., as a story of population growth.

Soon after the colony was founded there were troubles, such as, the historian would say, attend the birth of most States, and the population increased very little for five months or, say, twelve human years. Then the community entered upon

a golden age, the mortality declined, and the population steadily increased until by October 8 it consisted of 182 happy citizens, seven times its original strength, or, approximately, it had increased as much as the population of England and Wales increased between 1700 and 1911, and, like that increase, the upward movement was an affair of the last part of the time (in England and Wales population hardly increased at all between the time of Elizabeth and the last thirty years of the eighteenth century). But this happy state of affairs did not last. From October 8 the population began to decline inexorably; by March 4, 1922, there were only fifty left. Worse was to come; the numbers fell to scarcely more than the original twenty-six, but then there was a turn for the better, and on May 1, 1923, fifty-eight, a little more than twice the original strength, were alive. This first epoch of mouse history covered almost two years and two months. If we take a mouse year as equivalent to thirty human years (the average life of a mouse seems to be about two years), this corresponds to a history of sixty-five years. The average population was 63.5, and the mean immigration rate is therefore 4.72 per cent. per diem, or, in human ratios, per mensem, i.e., 56.6 per cent. per annum. This doubled the population in sixty-five years.

On May 1 a new immigration law came into force. Only one mouse was allowed to enter. When this law came into force the community was in the throes of an epidemic, but, as the historian would say, the firm measures taken had their effect, and, in spite of the reduced immigration—in consequence of it, as the legislators might have affirmed—the population increased and approached seventy by July, 1923. Fresh civil disturbances arose, however, and the population again declined and even dwindled to twenty-two, less than the original number; but matters improved, population increased slowly but surely, and on March 14, 1925, reached eighty-one. But the troubles were not over; from that point to the middle of June the community dwindled and actually looked extinction in the face; fell well below twenty. But again there was a recovery. By the beginning of July the census showed forty inhabitants, and in the last months of 1925 there was little fluctuation. On the last day of the year there were forty-two. Looked at from the historical point of view we can see that the legislation of May 1, 1923, was a mistake. In the seventy-five human years since then the population has fallen from fifty-eight to forty-two, and has for several years exhibited that stagnancy which, we have been assured, is so dangerous.

That is, in outline, the civil history of this State.

We shall now consider its medical history. During the first mouse-year pasteurellosis was not only the reigning but almost the only fatal disease, but at the end of the year *Bacillus aertrycke* (Mutton) got through our barrage (after the mischief was done it was discovered that a considerable stock of supposedly normal mice carried both *Bacillus aertrycke* and *Bacillus gaertner*), and this new disease has never been eliminated. It was, so far as the community were concerned, literally a new disease and unquestionably imported by immigrants. This intruder for a time secured epidemic control and the epidemic constitution changed from Pasteurian to Aertryckian. There were, in fact, between June 27, 1924 and January 5, 1925, no deaths at all chargeable to pasteurellosis. As in human terms, that is about fifteen years, immigration officers might reasonably have congratulated themselves that at last pasteurellosis was stamped out; but on January 5, 1925, a dead mouse exhibited the stigmata of both *Pasteurella* and *Bacillus aertrycke* infection. As, however, the Aertryckian Epidemic Constitution was then reigning in a vigorous way, no serious epidemiologist would have had any difficulty in explaining away the finding. But the Aertryckian constitution waned, and on March 12, 1925, a fresh series of pasteurellar deaths began to occur, and continued for just under three mouse months, or seven and a half human years. Aertrycke resumed control then, and since June there has only been one pasteurellar death (on December 14, 1925).

It is interesting to speculate, in the manner of Mr. H. G. Wells, alas, *longo intervallo*, as to how this series of events might have been interpreted by the mice themselves. There would surely have been a party favouring the tightening up of immigration control, indignant at the entrance of *Bacillus aertrycke*, enthusiastic supporters of the law of May 1, 1923, and almost offensively triumphant over the obvious consequences of firm public health administration during the next ten years. Probably they would have died before being proved false prophets. But, even if they survived they would not have lost prestige; they could have argued that the control of immigration was still incomplete.

There would also have been a few erudite mice; one conceives their transports of contemptuous amusement when the administrators of 1923 proclaimed the Aertryckian infection a new disease. "Have you," they would ask, "paid attention to the events of forty years ago, the strange sicknesses—it is very unphilosophical to talk about diseases—which were prevalent in the time of our ancestors, all far wiser mice than we; there is nothing *new* about these prevalences. Cease to chatter idly about novelty. When you fully comprehended the nature of the vast genii who at roughly periodic intervals transport us, in a manner still obscure, from one habitation to another, when you fully and exactly grasp the whole cosmos, embracing us mice, the genii themselves, and the larger genii which no doubt control *them*, you will have a right to call yourselves epidemiologists, and be sure that whatever you *do* discover will be no more than a tedious amplification of what our incomparable ancestors believed, as we—when you *have* made the discovery—shall not fail to mention." Lastly, there would have been a still smaller party of algebraical mice, sedulously analysing the records of mortality, who would not even have provoked contradiction, for their results would be unintelligible to all other mice, and they themselves mainly interested in criticizing each other's methods.

We think this experiment has taught us a great deal. In the first place it has, in our opinion, brought the doctrine of Epidemic Constitutions within the compass of rational inquiry. The successive waves of epidemic sickness have occurred in such a manner and at such time intervals (taking account of the differences of life-span of mice and men) as, in human medical history, gave rise to the doctrine of Epidemic Constitutions. In comparison with the real epidemiologist we have indeed had one disadvantage, viz., that our *clinical* observations were restricted to the fact of death; we knew nothing of the patients' symptoms. But we have had a great many advantages. The social and economic milieu has not changed, the rate of increase has been strictly controlled and, excepting the victims of cannibalism, all deaths have been certified with pathological accuracy.

The epidemic constitutions of our mice populations are not, we submit, directly or indirectly due to any occult and inexplicable change in the very bowels of the earth, as Sydenham would have it, nor to any super-meteorological phenomena, whether variations of terrestrial magnetism or any other of the high cosmic phenomena which some modern *Gelehrte* have advised us to study. They are certainly due to something happening in the population which we may not have wit enough nor live long enough to unmask, but which assuredly will be discovered by a suitable application of the statistico-experimental method. Of course *comparaison n'est pas raison*. Perhaps our epidemic constitutions are only pseudo-constitutions, not to be confused with the real Simon Pure. But since we *can* thus study the waxing and waning of epidemics associated with different micro-organisms under experimental conditions, which in absolute time have a rhythm on a different scale from that of human epidemic successions; since both rhythms cannot keep step with the high cosmic phenomena of Sydenham and his admirers, we shall adopt a Philistine pragmatism and jettison any interpretation of Epidemic Constitutions which cannot be subjected to experimental verification. We shall not ask to see it "on a plate" but we shall certainly ask to see it in a cage of mice.

We now return to the question whether this experiment throws any light upon the value of removing infective individuals from a community into which non-immunes are allowed to enter. We think it creates a presumption that such removal is, *from the point of view of the community*, largely futile.

It will at once be objected that we have never removed a single infected animal until he died, so that we have no parallel whatever with the practice of a human community isolating frank cases of infectious disease. But in this experiment there was a period of six months, equivalent to fifteen years, without a single death from *Pasteurella* infection, yet the infection revived without re-importation. It would, indeed, be remarkable isolation of, say, scarlet fever, which could place a human community for fifteen years in so favourable a position from the point of view of reduction of infective material. Yet the disease was not conquered. This is not a solitary instance. We have two other experimental colonies, each started by twenty pilgrim (and infective) fathers, and each continued for nearly two real years, say sixty human years. They were both inaugurated on February 14, 1924; in one (we call it Experiment 5), one mouse had been added every second day, the other (Experiment 6) has received an immigrant every third day. In neither population has the purity of the experiment been troubled by the incursion of any other infection. The histories of the two colonies are these. Experiment 5 began with four small waves of mortality and then enjoyed a quiet interval of two months (say five human years) during which the population reached forty, double its original strength. Then another epidemic began and in September–October, 1924, the population fell below its original strength. It recovered to nearly thirty in the early spring of 1925, but an epidemic in June brought it down to seven, when it began to increase, and in December, 1925, had reached 37. In the epidemic waves nearly all the deaths were definitely proved to be caused by pasteurellosis.

The history of Experiment 6 is more remarkable. As in the other communities there were increases of mortality after colonization, but no important movement until July, 1924; the colony passed through this crisis and in September had twenty-five members, five more than the original number. By January, 1925, this population had been reduced to 15 when it began to increase, reaching 30 on February 5, and remaining about that figure until March 19, 1925, when it again began to fall to twenty-one, but recovered to thirty by the second week of June, 1925, at which date a new epidemic began and reduced the colony to six. There was once more a recovery and in October, 1925, the population reached thirty-two, but fresh epidemics had reduced it by December 31 to less than ten.

A Malthusian mouse might use this history, the reaction of the colony to over-population by the positive checks of pestilence, to enforce the law that population always presses upon the limits of subsistence. The epidemiologically interesting point is this. Between July 20, 1924, and June 11, 1925, that is, over an absolute period of 325 days, almost twenty-eight human years, not a single death due to *Pasteurella* infection could be proved to have occurred. The last survivor of the July, 1924, epidemic of pasteurellosis died, having been a member of the colony 64 days, on May 26, 1925, 17 days before the new epidemic of pasteurellosis began (unfortunately he was one of those not able to be examined post mortem).

This experiment confirms the inference we drew from the long latent period in the main experiment.

It is, we think, fully established that a population wherein such an infection as pasteurellosis exists or has existed will probably never be rid of the disease again *if* it admits healthy immigrants. Merely excluding infective immigrants will never suffice to eliminate the disease.

The critic will at once retort that this in itself shows that our experiments throw no light upon at least one great problem of epidemic disease. Bubonic plague has died out in England and Wales. Whatever we may say about at least some of the

fourteenth century plague, however much of it may have been primary pneumonic, there is no doubt at all that the plague of the sixteenth and seventeenth centuries was ordinary bubonic disease. Therefore there must have been vast numbers of infected rats. Rats are constantly receiving new immigrants, *per vias naturales*. Why is not rat plague going strong all over England to this day? We cannot answer that question, and will not evade the difficulty by a reference to the partial replacement of the black rat by the brown rat, nor by throwing the onus of explanation upon mutations of the *materies morbi*, although both these factors may be concerned. We shall keep to a factor within our sphere of observation, the study of which seems to be important. This is the ratio of potential susceptibles to potential (or actual) sources of infection. Some of our best epidemiologists have explained the periodicity of, for instance, measles epidemics by the arrival at a critical value of the ratio of susceptibles to infectives. Sir William Hamer expressed this hypothesis in quantitative terms in his Milroy Lectures of 1906. Dr. Brownlee, while not accepting the explanation, for reasons which are important, recognizes that it covers at least some of the facts and that we can in this way explain some important epidemic phenomena. The study of the spread of infection within houses, which we recognize may perhaps not be strictly relevant, suggests—it does no more, for the exact data are scanty—that the increase in the proportion of susceptibles has a different effect in different diseases. All would agree that measles is much more infectious (we are not quite sure that all would agree on a precise definition of “infectious”) than scarlet fever. It is at least quite certain that when susceptibles are exposed to frank cases, the proportion of the former going down with the disease is very much greater, at least—five times greater—in measles than in scarlet fever. Now, Dr. McClure’s extensive Manchester data, covering more than 15,000 cases of scarlet fever, showed that as the proportion of susceptibles in a house increased the proportion attacked did not sensibly change. In houses with one initial case and one susceptible the proportion of susceptibles attacked was sensibly the same as in houses with one initial case and three susceptibles. In some very careful records of houses with an initial case of measles which one of us compiled from the admirable manuscript data of our lamented colleague, Dr. Reginald Dudfield, the proportion of attacked susceptibles decreased as the number of susceptibles per house increased. In our experimental work regular increase of the number of susceptible immigrants from one every third day to six every day increased, almost regularly, the rate of mortality and diminished the intervals between the epidemics. In the population of mice receiving six a day, it looked as if—unfortunately this experiment was ultimately spoilt by the intrusive *Bacillus aertrycke*—had it been possible to keep the experiment going on we should have smoothed out the waves and maintained a high and fairly steady death-rate. In other words, that we should have reached a point at which, epidemiologically, the supply was just equivalent to the demand. What would have happened had we increased the supply *beyond* that point would have been a very interesting matter. We hope to examine the question again. We have at least not reached an upper limit of mortality by the method of continuous addition, i.e., so far increasing the quota of regularly arriving susceptibles increases the rate of mortality. But when we proceeded on another tack and introduced into a community not small batches of regular immigrants but large parties at long intervals, the epidemic mortality was low.

We started here with twenty settlers mingled with eighty immigrants (it will be remembered that the settlers came from an infected stock) on February 14, 1924. Eighty more immigrants were added on March 19, fifty on May 3, fifty on June 11, and fifty on July 1. At the beginning the death-rate was rather high. The first and, until the middle of August (i.e., after immigration ceased), largest wave of epidemic sickness lasted about a month; from the end of this the rate of mortality remained very low until some six weeks after the admission of the last batch, when

the mortality began to increase and eventually reduced the population to two. As a *Bacillus aertrycke* infection developed just before the arrival of the last fifty immigrants, the experiment is neither clean enough nor was continued long enough to be very satisfactory, but some points emerge. Although after the admission of each batch of immigrants the death-rate began to rise at the end of a few days the increases were quite small, and the average pasteurellar death-rate was low although the mean population was large, the second largest in our series. A sudden and great increase of the ratio of susceptibles to potential infectors did not lead to a violent epidemic. The conclusion we draw from this is that to ensure a high epidemic rate it is not enough to have a large susceptible population at risk and, conversely, that the comparatively healthiness of our small colonies admitting few immigrants was not a mere consequence of their small numbers. Perhaps some will suggest that the analogy is with a fire; put a few coals on it regularly and it burns brightly, empty the coal scuttle into the grate and it goes out. But the analogy is very crude, and we think a good deal more work must be done. We do not know of any exact studies on the effects of school openings after the holidays distinguishing schools of different sizes; they might be suggestive.

At present, all we think we know is that not the number of the susceptibles at a given moment in proportion to the infected or any simple function of that ratio determines the moment of an epidemic. The old tag, *gutta cavat lapidem non vised sæpe cadendo*, seems to apply. We would sooner admit 1,000 susceptibles to a herd at once than ten a day for a hundred days if we desired to keep down the rate of infectious disease.

We now come to a matter our investigation of which has hardly passed beyond the preliminary stage, viz., why does an infectious disease come to a temporary end? There are, at least, four theories. One is that the susceptibles are exhausted another that an active immunity is established; a third that the "epidemic constitution" changes; and a fourth that the organism ceases to be infective.

So far as our little cosmos of mice is concerned, we have given reasons for holding that the doctrine of "epidemic constitutions" in Sydenham's sense can explain nothing, so we rule it out. Dr. Brownlee's intellectual child, the changing life cycle of the parasite, is a sturdy infant to whom we may ultimately offer chocolates, but at present we do not quite understand his language and are not sure that he wants our chocolates. The two other theories *seem* easier to test, although we have got but a little way towards testing them.

This is the way we have gone to work. We established two colonies rather more than a year ago. Colony A was designed as a sort of purgatory. *Pasteurella* was established in it and clean immigrants introduced (the precise numerical details will be given elsewhere, they are not material to the present brief discussion). Another, Colony B—whether analogous with heaven or hell is doubtful—was recruited from two sources, (a) from mice who had passed through the purgatorial flames of A, (b) from pathologically blameless immigrants in all respects comparable with the immigrants of our other experiments. The matter for study was the fate of the two classes in B. Down to the time of writing many more than a thousand mice have entered B, either from A, or from a state of innocence (we call the latter C mice), and there is not the least doubt that, on the average, A mice live a good deal longer under B conditions than C mice. Thus, if we take as a measure the proportion of immigrants to B who lived at least twenty-eight days in B, this was 23·3 per cent. for C mice, 26·7 per cent. for mice who had lived ten days in A, 36 per cent. for mice who had lived twenty days in A, and as much as 55·6 per cent. for mice who had been able to stand purgatory forty to forty-five days.

If we took as a measure the average number of days lived from entry to B to death, there was the same superiority of the A's with this difference, that there was a tendency—we cannot put it much higher—for the superiority to increase to a

maximum with increasing sojourn in A and then to fall off. Thus in one series of entrants to B on a particular day, the C's lived on the average 34.1 days; the A's, with 10 days' experience in A, 41.3 days; those with 20 days' 53.6; those with 30 days' 49.6; and those with 40 days' only 16.7. Now the mere superiority of the A's might be equally well explained by the exhaustion of susceptibles or by the acquirement of immunity. The A conditions may have killed off the most susceptible, so that only the fittest are exposed to B conditions, hence their superiority to the unweeded sample of C's. Or mice are born epidemiologically equal and those who went through A were actively immunized. We see no reason to believe that either explanation is the whole truth, but what we do want to know is, which factor is the more important? The point we made above, viz., that the superiority of the A's did not (in the matter of length of life) go on increasing with length of sojourn in A is clearly against the pure selection theory and in favour of the hypothesis of acquired immunity, but, having regard to small numbers and variability, is not decisive. An attempt to cut the knot failed. We argued that if we compared—not the average length of life of the C's, but—the average length of life of the best of the C's with the A's we might cut the knot. Thus, suppose of the A's in the batch entering A, whose survivors went to B, the total mortality were 20 per cent. in A. Let us compare the longevity of the 80 per cent. who survived to enter B—not with that of their companion batch of C's but—with the length of life of the 80 per cent. longest-lived C's in the batch. Now if such a comparison still gave an advantage to the A's, it would be a pretty clear proof that selection was not enough. But if it did not give the A's a superiority it would certainly not prove that only selection was at work, for the possibilities of active immunization are still present in B. Actually the average longevity of the A's was greater than that of the best C's so defined, 33.3 against 29.5 days, but in individual batches the best C's were longer lived than the A's as often as not. The test did not give an unequivocal answer.

Two other pieces of evidence, however, told in favour of immunization against selection. The first was that length of life in B was more highly correlated with length of exposure in A than with the severity of the death-rate during exposure in A. It was better to have survived a moderate time in A under mild conditions than a short time in A under severe conditions.

Also, when we separately studied the histories of A mice who had never been exposed to a high rate of mortality in A in conjunction with C mice, it was found that the advantage of the A mice increased to a maximum as exposure in A increased and then decreased, just as we should expect if immunization rather than selection were the prime factor.

The average length of life of the corresponding C's was 20.9 days, of A's with ten days' training, 23.3; with thirty days, 25.4; with fifty days, 34.6; and then a decreasing advantage. A's, with 71 days' exposure lived only 14.9 days in B.

Neither piece of evidence is decisive; this study is only beginning, but the balance is in favour of immunization rather than selection. We know of no human data giving the results of subsequent exposure to a common infection of groups of persons who have passed through, some a mild, others a severe, epidemic, others no epidemic at all. The data collected by the Ministry of Health in connexion with the great epidemics of influenza are the most nearly in point. From these it appears that there were five out of twelve instances where those who had influenza in the mild summer epidemic had a significantly lower attack rate in the winter phase, and only four instances where those attacked in the autumn had a significant advantage in the winter. In other words, passing successfully through the very severe autumn disease did not, on the average, confer more protection than passing through the mild summer disease. For obvious reasons this is a very loose analogy; as pointed out in the report, the problem of immunity against influenza is an excessively complicated one.

At this point we must break off the story of our experiments. Perhaps it will be said: "Your positive contribution to knowledge is very meagre. After years of labour, holocausts of mice, much arithmetic, much expenditure of money, you have only proved that in communities of mice a particular microbial disease will continue indefinitely if you introduce fresh susceptible individuals, and that the disease will wax and wane, being at times replaced by another microbial infection, in a fashion similar to what occurs in human experience. You have made it probable that the form of the secular curve of epidemicity is dependent upon the rate of addition of susceptibles and that an acquired immunity as well as selective immunization have a part in the advantage survivors of one epidemic enjoy when exposed to another. All these things any reasonable man might have inferred from human experience. We know that measles has been endemic-epidemic since the days of Edward III and mumps since the time of Hippocrates. We know that persons can be actively immunized against diphtheria and that some families and, indeed, some races are far more susceptible than others to zymotic disease. Was it really worth while to spend so much time and money in demonstrating these notorious facts?"

We shall not rely as, for forensic purposes, we might upon the retort that if the medical world does indeed know all these things, it certainly does not act upon the knowledge, but still proceeds, at great expense, to act on the belief that epidemic disease can be controlled by the temporary segregation of sick human beings or the slaughter of sick beasts. We shall not rely upon that retort, since the obvious fact that hardly anybody is a consistent Christian is not a logical proof that Christian ethics are unsound.

Our defence is based upon the principle that no problem can be solved until it has been clearly enunciated, and that the problem, or group of problems, covered by the word epidemiology has never yet been clearly enunciated.

*Sed nil dulcius est, bene quam munita tenere
edita doctrina sapientum templa serena,
despicere unde queas alios passimque videre
errare atque viam palantes quaerere vitae.*

The administrator, or public health official (termed by his critics an office epidemiologist), the students of medical history and statistics (termed by their critics arm-chair philosophers and "mathematicians"), have all realized the sweetness of this position and been led by self-esteem to imagine that they are in truth occupants of heights of serene wisdom from which they can survey impartially the phenomena of human epidemic disease. But, in fact, neither an established civil service post, first-hand acquaintance with the writings of Ballonius, nor even a working knowledge of the theory of multiple correlation, is an adequate safeguard against the weakness of human nature, conscious of the fact that those whom we see from the heights, "wandering all abroad and going astray in their search for the path of life," are human beings, whose passions we share and whose applause we covet. They return to our serene questionings a great variety of answers, and we generally catch the answer we wish to hear. But even in these humanitarian days the calamities of mice do not stir our feelings over-much; mice cannot assure us that we are energetic administrators, philosophical scholars, or skilled mathematicians. The problems that their lives and deaths afford we can formulate with a decent objectivity.

In the course of this work we have presented to ourselves, although we may not have the literary art to present to others, a far sharper picture of the march in time of an epidemic disease than the confused palimpsest of human experience has given us. We seem to begin to understand the mechanism of the epidemic movement and the nature of herd immunity, how it is established and how it is lost. We perhaps shall not live to know enough of the mechanism to turn it to a practical account, but we have faith that when experimental epidemiology, now an infant, is full grown, the occupants of the *templa serena* will see the struggling masses below less confusedly, having learned what to look at.

Sir LEONARD ROGERS exhibited a number of charts illustrating the influence of climate on the prevalence of small-pox in India.

Discussion.—Dr. A. BALFOUR said that, after listening to this learned and philosophical paper, he felt that, unless one belonged to the class of "erudite mice" or to that of the "algebraical mice," or possibly even to both, it was not easy to discuss it to advantage. He did not belong to either of these groups, and hence did not feel competent to comment on the paper, but he would like to put some questions. Dr. Greenwood's remarks on plague in this country had specially interested him, and he wondered if d'Herelle's bacteriophage had played any part in bringing the great epizootic in this country to an end. Quite recently d'Herelle had isolated a lytic principle from the faeces of rats during a plague outbreak in China, had cultivated it, and even used it at Alexandria in the treatment of bubonic plague. He suggested that Dr. Greenwood and Professor Topley might look into this question of a bacteriophage in the case of these mice epidemics if they had not already done so. He recognized, however, that they probably had more than enough to engage their attention. The hypothesis that the bacteriophage might play a part in terminating epidemics had, of course, been advanced. He would like to know what was meant by a "normal mouse population." They had heard about the control colony of presumably healthy mice, but deaths did occur amongst these mice, and it would be of interest to hear about the causes or mortality, as these might prove disturbing factors during the epidemics of *Pasteurella*, *gaertner* and *aertrycke* infections. He hoped that some day Dr. Greenwood and Professor Topley would turn their attention to yellow fever, a disease which presented interesting problems, although, of course, an insect intermediary had to be considered, and it introduced a complication to some extent.

Yellow fever was at one time endemic in St. Thomas, one of the West Indian islands, but it gradually vanished without any active steps being taken to hasten its disappearance. The island, at one time prosperous, had declined in importance, and, as a result, the influx of non-immunes diminished. The inhabitants had probably acquired a permanent immunity, and the number of non-immunes born in the island was not sufficient to keep the disease going. Such, at least, was the view held, and a useful comparison might be instituted between such an occurrence and the experimental work on mice. Of course yellow fever could not be transmitted to mice, but an examination of the historical and statistical data would be interesting and perhaps valuable. Again, take the large island of San Domingo. There had been no cases of yellow fever there since the early nineties of last century. Yet, before that time, the disease was present, and it had disappeared even though the island was in close touch with Cuba and other places when yellow fever was prevalent in them. No efforts have been made to combat the *Stegomyia* or to prevent the disease in any way. It died out spontaneously; why, no one knew. A consideration of this kind led him to think that possibly unknown factors might be present of which, at present, we knew nothing.

Dr. J. A. GLOVER compared the *Pasteurella* infection of Professor Topley's mouse population with the history of the meningococcus infection of the Guards Depot at Caterham, and he showed a graph of two of the four epidemic waves of carrier and case epidemics which had occurred there during the war. The Depot, with its large batch of additions of susceptibles, was most akin to No. 7 of Professor Topley's experimental series, and the Caterham graph (which, although it covered more than two years of human experience, was only equivalent to five weeks of Professor Topley's curve) showed distinct resemblances to some periods of that curve. By another diagram, in which years were superimposed, Dr. Glover showed that in the human community with meningococcus infection, environmental conditions, particularly overcrowding, were of greater importance than the cosmic influences of season and weather, highly important though the latter were.

Another point of resemblance to one of Professor Topley's experiments in which mice that had been previously exposed to infection were mixed with unexposed mice in a new community, was the fact that although the trained soldiers and the newly entrant recruits shared equally in the "carrier epidemics," not a single trained soldier suffered from meningitis; all the patients in the "case epidemics" being recruits.

It was interesting to note that in the Caterham graph the first wave (1917) shown was almost entirely due to Type II meningococcus. "Spacing out" and other prophylactic measures almost completely purged the Depot of this infection, and the second wave (that of 1918) was entirely due to Type I meningococcus.

Dr. E. W. GOODALL said that all epidemiologists were agreed that the number of factors concerned in the rise, continuance and fall of epidemics were often so many and complicated that it was extremely difficult to assign to each its proper share. Dr. Greenwood and Dr. Topley, therefore, by a most laborious and painstaking set of experiments and calculations were taking some of the factors singly so as to be able to ascertain as far as possible what part it played. He was of the opinion that so far as the infection with which they had worked was concerned they had made a most valuable contribution to the study of epidemiological factors and especially towards that of the increase of a population by the addition from time to time of susceptible individuals. He would, however, raise the question whether one could fairly argue from this particular set of experiments in order to explain epidemics in human populations of such diseases as influenza, small-pox and measles. He understood from a perusal of these and other papers by the same authors that the infections they used, *Pasteurella muris* and *Bacillus gaertner*, were infections which were taken in by the alimentary tract, as in the case of enteric fever amongst human beings. From his experience of what happened in children's wards and from what he had read of what happened in small isolated human populations, he considered that it was very doubtful whether it would be possible to keep such a disease, as for instance measles, going for the length of time the writers of the paper had kept their infections going amongst the mice. There was every reason for believing that such infections as measles, small-pox and influenza were taken in through the respiratory and not the alimentary tract. Some of the conclusions reached by the authors he had himself arrived at from an experience of nearly forty years in the administration of wards full of children, and especially that there was no surer way of keeping an infectious disease going in a ward (say measles in a diphtheria ward) than by admitting fresh susceptibles to fill any vacancies that might occur. Again, some of the mice in the experiments survived one or more epidemics only to succumb in a later one; so one saw children pass unscathed through one or two exposures to such a disease as measles and yet catch the disease on the third. The continuation of an infectious disease in a community might also depend upon whether it was a disease in which carrier cases were at all common.

These experiments also bore on the question of the acquisition of immunity by sojourn in a place in which a certain infection was more or less continuously in evidence. Some of the mice in these and similar experiments certainly did not become immune; apparently others did. While there was evidence that in human populations immunity to certain infections could be acquired in these circumstances—for instance to diphtheria, scarlet fever and enteric fever—there was none that he knew of, that immunity could be so acquired to such diseases as measles and small-pox. Here again it was possibly a question of whether the disease was or was not one in which the carrier condition could occur. He thought that the authors had rejected rather too lightly the variation of the infectivity of the micro-organism as a factor in the rise and fall of epidemics. The history of scarlet fever in this country in his opinion went to show that that variation was not an impossible factor, and more than one experimenter had shown that the passage of organisms through animals led to a diminution, certainly of its power of killing an animal and possibly of its infectivity.

The authors had touched on the question of the epidemic constitution. Their contention was right that that doctrine was brought within the compass of rational inquiry by such experiments as those they had undertaken. He was under the impression that that doctrine had ceased to be taught in this country soon after the middle of the last century, but it had recently been revived by very eminent epidemiologists and was, therefore, worthy of inquiry. We owed the term "*Epidemic Constitution*," that is constitution of the season, to Sydenham, for Hippocrates spoke only of the "*Constitution*." The Greek physician gave us a method of inquiry from which he himself obtained little if any results, because he had neither the time nor the material at his disposal. He evidently attached much importance to weather conditions as a cause of diseases, (as Sir Leonard Rogers had shown them that evening in respect of small-pox in India,) but he would have nothing to do with the mysterious. Sydenham, however, could not explain epidemics by weather or other natural conditions and, therefore, appealed to something outside or above them, and this he called the "*Epidemic Constitution*." But no clear definition of it could be found in his writings. It was for the modern revivalists with the accumulation of facts that they had at their disposal to explain the doctrine, but, in the speaker's opinion, they had invented only a super-constitution to that of Sydenham. Their attitude might be described in Fracastorius's words that those who invoked the occult had little trouble in ridding themselves of difficult problems; all they had to do was to look to the occult for the explanation.

The following observations were submitted in manuscript by Sir William Hamer and Dr. Forbes :—

Sir WILLIAM HAMER wrote: Of course those of us who love the rivers of Damascus do not like having to wash seven times in Jordan. But we rejoice, all the same, to find that the first lesson from the "uniform environment" (freed from human frailty and all cosmic influences) is that accumulation of susceptibles *does* (in part) determine periodicity, whatever the periodogram may say. An old friend of mine, who "knows his measles," notes that "this pasteurellosis is just measles over again!" And, as he says, "the problems which (we gather) are now to be faced by the new science are identical with those the old epidemiologists have been hard at work on since the Stone Age." In speaking thus, he is no doubt trying to adapt his history to the new time-scale of mouse epidemiology. He and I are, however, so fascinated by the abstract of the paper that we mean to wash in Jordan, even to seventy times seven, if that will cure us of our leprosy.

All the same, we feel there is some excuse for the old epidemiologists. How could they all describe epidemic disease—"varium et mutabile semper"—in precisely identical terms? True, there are a few so-called "stationary fevers," but far more epidemics of "unstable type." The most striking fact about the influenzas of history is that they have again and again been hailed as "new diseases." On the other hand, the charge that the primitive epidemiologists did not, from the outset, take the precaution of securing "unchanging social and economic conditions" must be regarded as proven. It is to be regretted that they just said, as Margaret Fuller was wont to do, "I accept the universe," and, in fact, took the world as they found it. But what an extent of ground, what stretches of time and space, their investigations have covered! A Westminster Abbey guide used to arrest the attention of American tourists, standing before Southey's memorial in Poets' Corner, by describing Lodore as a "waterfall in Cumberland about the same height as Niagara but not quite so broad." So, the mouse epidemiology is as high, no doubt, as the human, but as yet it is wanting in breadth. One word in conclusion: the authors of the paper confess that their "well laid scheme of mice" has already, like the schemes of the primitive epidemiologists, been affected by a disturbing influence—a Gaertner infection has surreptitiously crept in. They say, "This produced effects comparable with the phenomena which, in human experience, the doctrine of epidemic constitutions has been invoked to explain." The appeal must be to Sydenham. Would he, when a full 150 years' exclusive study of one stationary fever (pasteurellosis) was, at length, agreeably diversified by the appearance of a "new disease," have straightway jumped to the conclusion that "epidemic constitution" was in question? Would he not, rather, have declared that "the brief life of a single mortal would be insufficient" for the complete study of the inter-relationship, if any, between the two diseases? Time alone will show, so I shall continue, as before, to read all the works of Dr. Greenwood and Dr. Topley, hoping for the best; but, at my age, despite the rapid time-scale of mouse epidemiology, I cannot hope to live to be enlightened on the point.

Dr. GRAHAM FORBES wrote: Although, in the words of the poet, "the best-laid schemes of mice and men gang aft agley," such was not always the case, to judge from the very interesting and remarkable record of the experimental work to which they had just listened. Thanks to the ingenuity and perseverance of men and the compulsory co-operation of mice, the joint "schemes" had resulted in a considerable measure of success achieved towards the elucidation of epidemiological problems, if not actually in the eclipse of the impenetrable halo surrounding those "blessed" but mystifying words, "epidemic constitutions."

The absence of Surgeon-Commander S. F. Dudley, R.N., among others, from the evening's discussion was very much to be regretted; his "Study in Epidemiology of Scarlet Fever and Diphtheria," published by the Medical Research Council in 1923, and probably familiar to the majority present, was a piece of work of considerable value. His observations on the spread of the two diseases in a resident community, like those of Dr. Glover on cerebro-spinal fever, formed, from the human epidemiological standpoint, as near an approach as was conceivable to the mouse experiments with *Pasteurella* and *aertrycke* infections just described.

Therefore there could be little doubt that Surgeon-Commander Dudley's contribution could not have failed to add to the value of their discussion. His deductions leant strongly to the influence of acquired epidemic immunity as a factor to be reckoned with in explaining the spread of scarlet fever and diphtheria, if not of other diseases. There was much to be said in favour of his views. Moreover, one could not but be impressed by the attractive and ingenious

theory he had put forward of the principle concerned in epidemics, termed "the velocity of infection," and described as the resultant of the velocity of the reception of infection and of the velocity with which the mechanism of immunity was capable of destroying infecting agents.

Dr. TOPLEY (in reply) said that, of the two diseases which Dr. Greenwood and he had studied, the *Bacillus aertrycke* infection was almost certainly acquired via the alimentary tract, but all the available evidence suggested that mouse-pasteurellosis was a respiratory infection, so that, as regards its portal of entry, it might be regarded as analogous to such human diseases as influenza. In *Bacillus aertrycke* infection it was certain, and in pasteurellosis probable, that the majority of those mice which had survived any long exposure to risk had not escaped infection but had resisted it, and that many of them were harbouring the causative organism in their tissues. Dr. Greenwood and he had not rejected the possibility that variations in the biological properties of the parasite might play an important part in the course of events. There was no doubt that such variations did, in fact, occur under artificial cultivation. The question whether or not such variation played a significant part in the sequence of events they had described remained to be answered by future experiments.

The observations which had been made on the spread of cerebro-spinal fever during the war afforded the most interesting analogies to certain of their experiments, and the resemblance between the course of events which Dr. Glover had described at Caterham and the results obtained in certain experiments on mouse-typhoid was particularly striking.

A few experiments had been carried out on the effect of administering a bacteriophage, active against *Bacillus aertrycke*, to mice among which mouse-typhoid was actively spreading. The results had been uniformly negative, although the infection had a close general resemblance to fowl-typhoid, in which d'Herelle had recorded strikingly successful results.

Although there was a certain resemblance between the gradual immunization which appeared to occur among the experimental herds of mice, and the immunization which occurred during the spread of diphtheria among a human population, it would seem that very different factors must be involved, since the immunity developed by the mice appeared to be relatively imperfect and transient. It was possible that this was in part due to the difference between antibacterial and antitoxic immunity.

The study of the natural history of particular diseases in island communities, such as Dr. Balfour had referred to, would, if the data were adequate, be of the greatest service in determining whether the phenomena observed in experimental epidemics gave a true representation of the course of events in natural epidemics of disease among man.

Section of Epidemiology and State Medicine.

President—Dr. JOHN C. McVAIL.

Typhoid Fever in Northern Ireland.

By Professor W. JAMES WILSON, M.D., D.Sc.

PERHAPS one of the most striking facts emerging from British Vital Statistics is the extraordinary decrease of the deaths attributed in recent years to enteric fever. This satisfactory diminution of enteric mortality is apparently not confined to England, but probably prevails in varying degrees over the greater part of America and Europe.

In 1922 the enteric mortality rate per 10,000 of the population in the United States of America was 0·31, whereas in 1910 it had been 1·95. From the answers to a questionnaire submitted by the Committee of the Office International d'Hygiène Publique in October, 1922, I have compiled the following Table, and at the same time have added to it the figures for Ireland:—

TABLE I.—RATE OF MORTALITY PER 10,000 OF THE POPULATION.

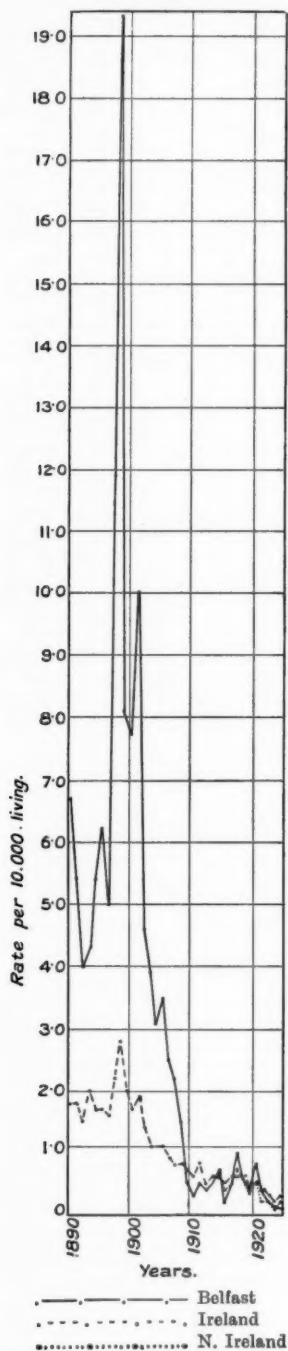
Country	Year 1891	Year 1921
England and Wales	1·68	0·16
Scotland	1·98	0·18
Denmark	1·5	0·10
Holland	1·38	0·18
Italy	6·31	2·63 (year 1917)
Switzerland	1·17	0·16 (" 1920)
Spain	6·14 (year 1900)	3·29 (" 1922)
Portugal	2·08 (years 1902-10)	1·87 (" 1918)
Ireland	1·8	0·39

The returns from France showed that the average number of deaths had declined from 5,000 in the years 1906, 1907, and 1908 to 3,000 in 1916. In Norway the average number of deaths in 1891-5 was 715 and in 1916-20 only 338. In Sweden (1890-4) the number of typhoid cases, which averaged 4,048, was reduced to 1,266 in 1921.

Ireland in the past century suffered severely from typhus fever and relapsing fever, and in many parts enteric fever claimed a large number of victims. Information as to the number of cases of "fever" (other than scarlet fever) is available from the reports to the Irish Local Government Board of the Medical Officers of dispensary districts. For example, in 1865, 1878, and 1909, the numbers reported were respectively 26,566, 10,945, and 1,170, and the corresponding populations were estimated to be 5,594,000, 5,282,000, and 4,386,000.

A record of the number of cases of enteric fever occurring annually in Ireland is far from complete, as there was great delay in adopting the Infectious Diseases Notification (1889) Act, and in some areas it is still unadopted. However, registration of deaths due to enteric fever has been carried out very efficiently, and from figures obtained from the reports of the various Registrars-General I have been able to construct the curves plotted out in Diagram No. 2, which show the mortality rate per 10,000 in England and Wales, Scotland and Ireland from 1871 to 1924. From

DIAGRAM NO. 1.



the curves we see that England and Scotland had until 1888 a much higher death-rate from enteric fever than had Ireland. In 1875 the rates per 10,000 of the population were for Scotland, England and Ireland, 4·6, 3·7, and 1·6 respectively. From 1875 to 1886 there was a decline in the rate in Great Britain, but practically no change in Ireland during this period. In 1886 the rates for Scotland, England, and Ireland were 1·9, 1·8, and 1·6. The rates in Great Britain remained more or less stationary until 1899, when a decline occurred in all three countries, being preceded in 1897 and 1898 by a very steep ascent in Ireland mainly due to severe epidemics in Belfast. From 1900 there has been a fairly steady decline, but more pronounced in Great Britain than in Ireland. In 1924, 0·10, 0·13, and 0·31 were the rates for Scotland, England, and Ireland.

With this preliminary setting of the problem, and before dealing with enteric fever as it has affected Northern Ireland, I may point out that in Ireland, relatively to England, there is a very large rural population, and that only in Dublin and in Belfast are there whole-time medical officers of health. In the other parts of the country the dispensary medical officer of any district acts as Medical Officer of Health, and as his average annual salary for this office is £10, one may infer that the importance of his sanitary duties is not over-estimated. Recently drastic changes have been effected in the Public Health Administration in the Irish Free State, and are being contemplated in Northern Ireland. Information as to the sanitary conditions of Dublin and Belfast can be obtained from the Annual Reports of the Medical Officers of Health, and as regards the rest of the country from the annual reports of the Irish Local Government Board. In the latter the medical inspectors of the Board were accustomed to review annually the sanitary conditions of their areas and to give an account of investigations made by them in connexion with any outbreak of an infectious disease. There can be no doubt that the assistance and advice afforded by these inspectors has been most valuable—although the local authorities frequently neglected to put into operation many of the recommendations made. In looking through these reports one is struck by the frequency with which milk is incriminated, or at any rate suspected, as being the infective medium. It is, however, only since the beginning of the present century that bacteriological examinations have been made and actual "carriers" discovered. Later in this paper I shall give an account of several outbreaks where fairly complete investigations were made; in the meantime I shall indicate how modern progress, at least in some cases, has tended to deprive large sections of the community of the protection against enteric fever afforded by their isolated position in rural areas. This was the introduction of the Co-operative Creamery Societies. Farmers bring milk to the creamery and take away the "separated" milk. This separated milk is frequently used for human food, and as the pasteurization at the creamery is usually inefficient, a whole countryside may occasionally be infected with enteric fever, the source of infection being either at a farm or at the creamery itself. One inspector reported the discovery of an ambulant case of typhoid amongst the workers at a creamery. One of the earliest instances of enteric fever traced to the consumption of separated milk was reported in 1906 by the late Dr. C. J. Clibborn. In this outbreak in a rural area there were between November, 1905, and January, 1906, seventy-two cases and thirteen deaths. In the following year Dr. Brendon McCarthy reported the occurrence of fifty cases of enteric fever which he attributed to the consumption of separated milk, and again in 1908 a still larger outbreak from the same cause in the same area. In reference to this latter outbreak Dr. McCarthy stated: "The D—e creamery has 315 suppliers all living in this area, and the number of houses of non-suppliers is 1,090. From January, 1907, to the end of December of the same year, the total number of houses in which typhoid fever was treated was sixty, forty-four of which belonged to suppliers and fourteen to non-suppliers. The percentage of houses attacked among suppliers and non-suppliers was 13·9 and 1·2

respectively." From these facts, which are similar to those connected with many other outbreaks traced to creameries, you can see how enteric fever can be disseminated over a countryside. The disease when introduced has been found to persist in a district for many years. In the great majority of these areas the Infectious Diseases Prevention Act, 1890, had not been adopted, and it was impossible to prevent milk from infected farms being sent to the creameries. In certain cases an effort was made to pasteurize the "separated" milk, but whether this was efficiently done at all times was very doubtful. It is fortunate that the butter produced has not been shown to have caused disease.

Creameries have undoubtedly been the cause, since the beginning of the present century, of hundreds of cases of enteric fever in rural districts in Ireland, and as hundreds of cases have cropped up in infected areas in the course of the succeeding years, it is very necessary that effective preventive measures should be available.

Of the 123 deaths from enteric fever which occurred in the Irish Free State in 1924, 29 appertained to urban and 94 to rural areas; in Northern Ireland the corresponding figures were 11 urban and 14 rural.

In connexion with the epidemiology of enteric fever in Northern Ireland the greatest problem is to explain the enormous number of cases which occurred in Belfast up to 1905, and the steady and rapid decline which has prevailed during the past twenty years. In 1907 the Irish Local Government Board appointed five sanitary experts to form a Commission to hold an inquiry into the cause of the high death-rate in Belfast, and in connexion with this work Dr. L. W. Darra Mair wrote a special report on enteric or typhoid fever in Belfast (1908), and in 1909 he communicated to this Section a paper on "The *Ætiology of Enteric Fever in Belfast in relation to Water Supply, Sanitary Circumstances and Shellfish.*"¹ The Commission concluded that the water supply was not responsible for the epidemic prevalence of the disease. The main reasons for this opinion were (1) that the outbreaks in Belfast were not of an "explosive" nature, (2) that the cases had no relationship to the distribution of any of the three different water supplies to the city, (3) that the fever was mainly limited to the quarters of the city occupied by the working classes.

Mair did not consider the general sanitary conditions of Belfast worse than that of most of the other towns and cities in the United Kingdom. He stated that although there had been, and still were, many serious sanitary shortcomings in Belfast, and the system of scavenging of privies and ashpits even then was exceedingly defective, it could not be contended that in a sanitary sense Belfast was on an altogether lower plane than other cities and towns in the United Kingdom. In fact, there could be no doubt that in some respects the evidence pointed the other way. Belfast (he said) was a town of rapid modern development—that is to say it was a new town—consisting largely of wide streets lined by rows of comparatively modern dwellings, the vast majority of which were self-contained, so that there was an almost complete absence of antiquated courts, alleys and common yards, such as might be seen in Dublin and Cork, and also in many of the older seaport towns in England and Wales.

"Slums" are rare in Belfast. Likewise overcrowding of persons in houses in Belfast may be said to be negligible in amount.

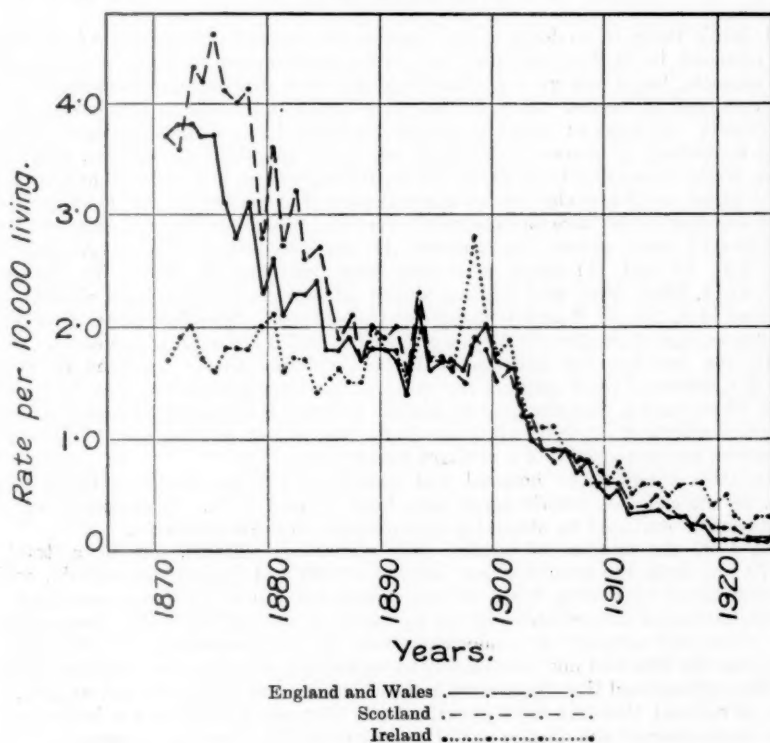
Mair concluded that the extraordinary incidence of enteric fever in Belfast could not be attributed to infected water, or to insanitary conditions, though the latter no doubt contributed, but that the consumption of shellfish collected from the polluted foreshore of Belfast Lough was a hypothesis which fitted best with all the epidemiological facts—many of which are summarized in Table II.

¹ *Proceedings*, 1909, ii (Sect. Epid.), pp. 187-242.

TABLE II.

Period	Population	Enteric fever mortality rate per 10,000	Death-rate per 1,000	Notable Events in the Sanitary History of Belfast.
1872-1875 ...	212,000 ...	7.0 ...	24.6 ...	Irish Public Health Act, 1878.
1876-1880 ...	230,000 ...	6.4 ...	23.7 ...	<i>Water Supply.</i> —From Woodburn up to 1890 when Stoneyford was introduced as a supplementary supply. In 1901 an additional supply from the Mourne Mountains was obtained.
1881-1885 ...	252,000 ...	4.0 ...	23.5 ...	In 1892 and 1894 the supplies from Stoneyford and Woodburn were filtered. In 1901 farms in the Woodburn catchment area were purchased and cleared.
1886-1890 ...	277,000 ...	6.0 ...	23.4 ...	<i>Sanitation.</i> —Scavenging of privies and ashpits was undertaken free by the Corporation in 1892. From 1880 to 1899 privies were being gradually replaced by water-closets. In 1899 only one-third of the total houses were provided with privies. Belfast Corporation Act, 1899, compelled owners to convert privies into water-closets.
1891-1895 ...	309,000 ...	5.0 ...	24.1 ...	In 1908 not more than 2,000 privies in the City. Between 1889-1895 a main drainage scheme was carried out and the sewage was diverted from the Lagan to Belfast Lough.
1896-1900 ...	349,000 ...	9.7 ...	22.9 ...	<i>Shellfish.</i> —In 1906 active measures taken against hawkers of shellfish and warning notices posted along the foreshores.
1901-1905 ...	372,000 ...	5.0 ...	20.0 ...	In 1906 the new Fever Hospital was opened.
1906-1909 ...	388,000 ...	2.0 ...	19.8 ...	In 1897 Infectious Diseases Notification Act adopted.
1910-1914 ...	392,000 ...	0.5 ...	18.3 ...	
1915-1919 ...	396,000 ...	0.5 ...	18.4 ...	
1920-1924 ...	428,000 ...	0.3 ...	15.0 ...	
1924— ...	434,000 ...	0.07 ...	14.3 ...	

DIAGRAM NO. 2.



In Diagram No. 1 the mortality-rates per 10,000 of the population are shown for Ireland and Belfast from 1890 to 1924, and for the Irish Free State and Northern Ireland from 1914 to 1924. The rates were in 1890 for Ireland and Belfast 1·7 and 6·7 respectively. The Belfast rate reached its peak in 1898 with 19·3, and its lowest level in 1924 with 0·07, when the rates for the Free State and Northern Ireland were 0·39 and 0·2.

Thus, from being the most infected city in the Empire, Belfast is now remarkably free from the disease. In 1924, only forty-three cases were notified, an attack rate of 1 per 10,000, and only three deaths occurred—a striking contrast to the 640 deaths which occurred in 1898, although the population was about 100,000 less.

It will be seen that Belfast in the early seventies had an excessively high mortality from enteric fever, that there was a diminution in the early and middle eighties, followed by a rise, which attained its maximum in the later nineties, and that since the beginning of the present century there has been a steady decline. Mair attributed the great elevation in 1897 and 1898 to the break-down of the "shoot" which, under the new sewage scheme, discharges the sewage directly into Belfast Lough instead of into the Lagan. The silting up of the distal end of the "shoot," and bursts near its origin, he believed led to a greater pollution of the shellfish, especially on the County Antrim foreshore, and the danger of their being specifically polluted was increased by the substitution of water closets for privies in the city—a sanitary reform which had made great progress in the nineties.

I think there is no doubt that a considerable amount of the enteric fever which has occurred in Belfast has been due to the consumption of contaminated cockles and mussels, but I am very doubtful whether the extraordinary decrease which has occurred in recent years is due to a complete change in the habits of the population. In spite of warning notices and of seizure of the supplies of hawkers there is nothing to prevent individuals collecting supplies for their own use; there is no doubt, however, that since the sedimentation of the sewage in tanks and the disposal of the sludge by its conveyance out to sea beyond the confines of the lough the foreshores have become much cleaner. Moreover, the reclamation of the foreshore at many places has rendered the shellfish less abundant. Amongst 83, 151, 106, 51 and 117 cases of enteric fever occurring in Belfast in the years 1909, 1913, 1914, 1915 and 1921 a history of recent consumption of shellfish was obtained in 1, 15, 15, 2 and 6 instances respectively. Shellfish were therefore a possible source of infection in 39 out of 508, i.e., in 7·6 per cent. of the cases.

In my opinion the decrease is to be attributed to the abolition of privies and the substitution of ashbins for ashpits, the improved scavenging, the abatement of nuisances, the decrease of stables and byres and their concomitant flies, the more effective sanitary administration, the higher standard of living and of education, and the growth of a sanitary conscience.

In 1906 a new fever hospital was opened, and since that date 50 to 90 per cent. of the cases of enteric fever have been treated in it. The sewage of this institution is sterilized by steam before admission to the city sewers.

In 1897 the number of houses with privies was 26,620, out of a total of 67,479; in 1902 the numbers had become 10,000 and 77,788 respectively, whilst in 1908 there were only 2,000 privies remaining. In recent years practically all privies have been converted under the Belfast Corporation Act, 1899. Scavenging of the privies and ashpits was undertaken free by the Corporation in 1892, and at that time the filth had not infrequently to be removed through the dwelling houses.

Mair appreciated that there were facts which his hypothesis did not explain, and that he realized that the rapid growth of the City might have been a factor in the great prevalence of the disease would appear from the following statement: "It is

possible that the diminution of fever which marked the first two years after 1901 may have preceded somewhat any very great reduction in the consumption of shell-fish. The point was difficult to establish with exactitude. The question arises, however, whether this earlier diminution of fever may not have been due, in part, to exhaustion of susceptible material among the population. It is a fact that about this time the Belfast population was not increasing at anything like the same rate as previously: indeed, it is probable that in 1901 and 1902 the population diminished somewhat. With this relative stagnation of the population, the enormous incidence of fever during the critical period of five years—there had been a total of nearly 19,000 cases, or about 5 per cent. of the population—suggests that for a time insusceptibility might have been a not unimportant factor in effecting a diminution of fever."¹ The work of Topley and Greenwood and their colleagues has demonstrated, in connexion with mouse typhoid, the great influence effected on an epidemic by the immigration of susceptible individuals into the cages." Topley, in a recent lecture, states: "When the pre-epidemic stage has been passed and a definite epidemic prevalence of the disease has been established, the future course of events is largely determined by the rate of immigration of susceptible hosts. If no such immigration occur, the epidemic gradually dies down, leaving a varying number of survivors."

"If susceptible animals be added regularly to the herd the form of the fluctuations in the resulting death-rate, and its average value, is mainly determined by the rate of immigration. With a moderate immigration-rate the deaths tend to occur in a series of well-marked waves without any quiet interval. If the rate of immigration be diminished, the waves of mortality tend to be more widely separated from each other, the intervening quiet intervals sometimes lasting over several months. If the rate of immigration be increased, successive waves of mortality tend to become fused together. The average death-rate may not be so high as that observed at the peak of a wave of mortality during an epidemic in which the immigration-rate is much lower, but the fusion of waves results in a high and relatively steady death-rate."

Now facts such as the above probably have a very direct bearing on the problem of enteric fever in Belfast. I am not in a position, nor have I the necessary data, to determine the effect of immigration on Belfast's enteric mortality, but it is perhaps not without significance that the highest mortality prevailed during the periods of most rapid expansion. The increase of population was due not merely to an excess of births over deaths, but to an immigration (1) from rural areas of large numbers of individuals and families; and (2) from Scotland of many shipyard workers and their families. The areas which were most infected were those in which the shipyard and factory workers mainly resided. The growth of Belfast during the fifty years between 1851 and 1901 was remarkably rapid, the population at the end of the period being quadrupled. The census figures were:—

					Percentage intercensal increase
1851	87,062
1861	121,602	...	40
1871	174,412	...	43
1881	208,122	...	19
1891	255,950	...	23
1901	349,180	...	36
1911	385,492	...	10.4

The returns of new buildings erected in Belfast annually, from 1856 to 1906, are available and tell the same story of rapid growth; the year which showed the largest number of houses erected (4,547) was 1898 and it is perhaps more than a coincidence that in this year enteric mortality was at its worst. The numbers of artisans' new

¹ *Proceedings*, 1909, ii (Sect. Epid.), p. 217.

² *Ibid.*, 1926, xix (Sect. Epid.), pp. 31-44.

houses erected in Belfast in the years 1897 to 1901 were 941, 1,207, 1,179, 947 and 548 respectively—an average of 964 per year: while in the years 1902 to 1906 the numbers were 195, 151, 130, 75 and 126 respectively, an average of only 135 per year.

We have already seen that in the seventies the enteric mortality in Great Britain was double that of Ireland, and, no doubt, that of the cities and towns was much greater than that of the country generally. It would seem reasonable to believe that Belfast, as late as the nineties, was passing through a phase which had been passed through some thirty or more years earlier by the towns and cities on the other side of the Channel.

Northern Ireland had, in 1924, in an estimated population of 1,279,000, 20,299 deaths, 10,537 and 9,762 occurring in rural and urban areas respectively. The death-rate was therefore 15·9, and about half the deaths occurred in urban districts. The deaths from enteric fever in 1924 numbered twenty-five, eleven being urban and fourteen rural. Belfast, with a population of 434,000, contains over one-third of the inhabitants of the province.

The Irish Free State in 1924 had a population of 3,161,000 and a death-rate of 14·29.

The enteric fever mortality-rate per 10,000 for the two divisions of Ireland, for a period of ten years, was as follows:—

	1914	1915	1916	1917	1918	1919	1920	1921	1922	1923	1924
Irish Free State ...	0·66	0·58	0·67	0·61	0·60	0·41	0·56	0·44	0·30	0·45	0·39
Northern Ireland ...	0·64	0·47	0·55	0·72	0·63	0·45	0·51	0·29	0·20	0·16	0·2

Up to 1920 the enteric fever mortality rate in the two areas was very similar, but since 1921 the rate in Northern Ireland has decreased more rapidly than that of the Free State and is now only about one half the amount of the latter.

Northern Ireland, on account of its small size and with a population half rural and half urban and with a Government of its own responsible for its health, will afford an opportunity for the thorough investigation of disease. At present a Commission is considering, amongst other questions, the subject of local government in relationship to health. No doubt as a result the sanitary organization will be brought more into line with that of Great Britain.

But even as it is, with only one whole-time medical officer of health in the province, the great assistance rendered to the part-time medical officers by the medical inspectors of the Ministry of Home Affairs, has compensated for the absence of whole-time officers and has limited the dissemination of infectious diseases.

In my opinion the work of the inspectors of the old Local Government Board in Ireland, and of their successors in Northern Ireland, has contributed greatly to the decline of enteric fever in the island both north and south. Reports of outbreaks are now promptly made and the advice of the inspectors has led to better diagnosis, the employment of bacteriological investigations, the improvement of sanitary conditions and of water and milk supplies.

I shall now give a brief account of some outbreaks which have occurred and in connexion with which, as Bacteriologist to the County Councils, I took some share in the investigations. Some of these illustrate the important part played by "carriers," about whose rôle some epidemiologists appear still to be sceptical.

I may mention in passing that it was in Belfast that my colleague, Dr. T. Houston, in 1899 discovered the first chronic typhoid carrier. This was a case of cystitis due to infection with the *Bacillus typhosus*.

In 1906 there was a small outbreak of enteric fever in the Windsor district of Belfast. The twenty-three cases which occurred in this residential area had a common milk supply. One of the milkers who was thought to have had an attack of influenza a short time previously was found to give a positive Widal reaction and was in all probability an effective "carrier."

This little epidemic, occurring amongst the richer class of the community, attracted a good deal of attention, and it emphasized the importance of serological and if possible bacteriological investigations where the circumstantial evidence suggests that milk is the infective vehicle.

A milk-borne epidemic which occurred at the latter end of December, 1910, and which was very fully investigated by the late Dr. Brian O'Brien, an inspector of the Irish Local Government Board, has several points of interest. The scene of the outbreak was a small village, D—y, consisting of 130 houses and with a population of 800, practically all employees of a large weaving factory. The houses were modern and the majority possessed water closets. The first case was notified on December 24, 1910; the second case was that of the driver of the milk cart, who was medically examined on December 22 and sent to bed, a diagnosis of enteric fever being made on December 27. The Medical Officers of Health, Dr. Frier and Dr. Boucher, had already, on December 25, stopped the milk supply; in fact, that day's supply was only partially consumed, as the dairyman, Mr. H., went round to his customers who had got their morning supply and urged them to destroy it as it was probably infected. I think this action on the part of a dairyman whose milk is under suspicion is unique, and it is sad to relate that he himself later developed the disease and died. There were thirty-six cases in all, twenty-five being in the village of D—y, eight at M—n, a small collection of houses half a mile from the village, and three at the milkman's house, situated two miles from D—y. The one factor common to all was the milk supply. The source of infection proved to be a servant girl who came to the farm on November 15, 1910. This girl had an attack of enteric fever in December, 1908, and curious to note she was infected by a former mistress who was a "carrier," and, as a landlady of a small hotel, had infected several of her guests. In 1910 another employer of this girl had an attack of enteric fever. Typhoid bacilli in large numbers were found in her stools, and though she was treated in hospital for many months with vaccines, intestinal antiseptics, &c., she remained a "carrier."

The suspected milk was supplied to sixty-six houses, with an aggregate number of inmates of 355. Twenty-four houses were infected and there were thirty-six cases of enteric fever, giving a morbidity rate of 10.1 per cent. No case occurred among the 400 people who did not obtain milk from the suspected dairy. Three of the patients died, including the dairyman and the driver of the milk cart.

An outbreak, in which water was probably the infective vehicle, occurred at B—a, an urban area with a population of over 11,000. On August 1, 1914, two cases of enteric fever were notified, and by August 14 the notifications had increased to twenty-eight, and by the end of September the number was seventy-two; a few more cases occurred in October and November. The water entering and mixing in the mains came from two sources: (1) An upland surface reservoir, and (2) an underground source in an iron ore mine. A bacteriological examination showed that the reservoir water was pure but that the mine water contained *Bacillus coli* in 0.1 c.c. That this mine water was probably infected was shown by the fact that two cases of enteric fever occurred amongst its consumers near its origin; their residence was several miles from B—a, with which they had little communication. Moreover, when the mine supply was cut off the epidemic ceased and the town has had few cases of the disease since 1914.

An outbreak which occurred amongst the members of the Church Lads' Brigade Football Club, Lisburn (an urban district 10 miles from Belfast) was traced to the consumption of a dinner in Belfast, and at the same time revealed the source of infection of some cases of enteric fever which were occurring simultaneously in Belfast. From a report on the outbreak submitted to the Ministry of Home Affairs, Northern Ireland, by Dr. John McCloy, medical inspector, I abstract the following facts.

Fourteen Lisburn lads visited Belfast on December 28, 1921, and after a football

match with a team of sea cadets, were entertained to dinner by the latter in their hall. This was the only meal which the Lisburn boys had together. The dinner party included forty sea cadets, fourteen Lisburn lads, thirty members of the cadets' committee and friends, and forty seamen, mostly members of the crew of the *S.S. Manhattan*. Before the source of the outbreak was discovered the *Manhattan* had sailed, and whether any of the crew contracted enteric fever is unknown. Among the remaining eighty-four members of the party, thirty-nine cases of illness occurred—twenty-three being enteric fever, two doubtful enteric, and the remainder influenza—a disease which was prevalent at the time. There were, therefore, at least twenty-three cases of enteric fever, eight occurring amongst the fourteen Lisburn lads, of whom three died. There was one death among the remaining fifteen cases. The onset in the majority was round about January 14—the earliest and latest cases developed on January 3 and January 27.

One of the two women cooks responsible for the meal had had a serious attack of typhoid fever thirty-eight years earlier. At the time of the inquiry she had a vague illness which was not clinically like enteric fever, but her blood gave a positive Widal reaction and her stools were found by Dr. N. C. Graham, the Belfast City Bacteriologist, to contain enormous numbers of typhoid bacilli. It is probable that this woman was a chronic "carrier," and that her illness was not due to an infection acquired at the same time as the others, but was due to an increase in the infectivity of the bacilli in her system. In my experience chronic "carriers" not infrequently show evidence of a modified relapse, e.g., malaise, fever, jaundice, &c. This woman had come to Belfast in August, 1921, and no suspicion as to her being the cause of enteric infections had arisen.

The outbreak is of interest in showing that, in cases of enteric fever where no apparent cause can be found, a source of infection may exist and only be brought to light by a favourable accident. On this occasion, but for the outbreak amongst the Lisburn lads, the source of infection in the Belfast cases would have remained obscure.

An outbreak which occurred in Belfast in the early months of 1925 again shows the dangers of infected milk. To a report of Dr. N. C. Patrick, medical inspector, I am indebted for the following notes.

From March 3 to March 17, twenty-six cases of enteric fever were admitted to the City Fever Hospital, twenty being received between March 11 and March 17. Of the twenty-six cases twenty were traced to a common milk supply—a dairy in the Antrim rural district, the milk of which was distributed by eight retailers. At the farm the owner was found to have had a prolonged attack of enteric fever, and, in fact, died from perforation on February 20. During his illness and for some time after his death the milk continued to be sent in to the city. In addition to the twenty cases, twenty-six other cases occurred subsequently, and were traced to contact with the previous cases.

From the investigations of enteric fever in Northern Ireland in recent years, of which the above are but a few examples, I am impressed with the importance of a thorough search for a source of infection being made in every case by a *trained* official. Only by means of data thus acquired will it be possible to draw general conclusions. It is satisfactory that enteric fever is declining, but there is every indication that if preventive measures were relaxed the smouldering ashes would soon cause a great conflagration.

Many points naturally still remain obscure, for example, why in Belfast the disease has become comparatively rare in spite of the large numbers of chronic "carriers" which must exist in the population. No doubt when more is known of the life history of the typhoid bacillus an explanation will be forthcoming.

I have pleasure in acknowledging my great indebtedness to Dr. H. W. Bailie, Superintendent Medical Officer of Health, Belfast, and to Lieutenant-Colonel W. R.

Dawson, M.D., Chief Medical Officer of the Ministry of Home Affairs, Northern Ireland, for much of the information on which my paper is based.

REFERENCES.

The Reports of the Registrars-General for England and Wales, Scotland, Ireland, Saorstát Éireann, and Northern Ireland. The Annual Reports of the Superintendent M. O. H., Belfast. Belfast Health Commission's Report to the Local Government Board for Ireland, 1906. DARRA MAIR, L. W., Proc. Roy. Soc. Med., 1909, ii (Sect. Epid.), p. 187. Office International d'Hygiène Publique, 1923, Bulletin No. 9, tome 15. TOPLEY, W. W. C., Lancet, 1925, i, p. 477. HOUSTON, T., Brit. Med. Journ., 1899, i, p. 78.

Discussion.—Sir WILLIAM HAMER said that Dr. Greenwood and Dr. Topley had set the example of collaboration, and that there was much to be gained by the closest co-operation between bacteriologists and epidemiologists. He (the speaker) had been greatly impressed with that fact when, as a young man in Dr. Klein's laboratory, he had had some opportunities of seeing how, in the early nineties, Dr. Klein and Mr. W. H. Power were accustomed, so to speak, to work hand in hand. The cockle origin of the Belfast typhoid was very securely established. The late Dr. Darra Mair, in his report, had disposed successfully of various criticisms. As regards the finding that only thirty-nine out of 508 cases (7·6 per cent.) were admittedly due to shellfish, it was clear that, in view of all the efforts made to prevent polluted cockles being consumed in Belfast, those who recklessly defied the authorities and took risks were not likely to be willing to "plead guilty" when called to account. Apart from this, there was, as Professor Wilson had said, the huge diminution in the amount of specific pollution, in view of the fact that the deaths from typhoid in 1924 were only one-hundredth of the number in 1898. It was much to be desired that further knowledge should be acquired as to the extent to which populations, affected to varying degrees by typhoid fever, were apt to yield evidence of including persons who were carriers of typhoid bacilli. The paper showed that there was one conundrum which troubled many of them, and was at the same time also a puzzle to Professor Wilson. When Darra Mair's paper was read, in 1909, many of his hearers felt that the limitation of the outbreak to the poor of Belfast was very difficult to reconcile with the bacillus carrier hypothesis. Dr. Mair was asked whether any active steps had been taken with regard to the hundreds of carriers in the city—cooks, housewives, handlers of food of various kinds—whether urotropin had been extensively administered or cholecystotomy practised on a large scale. The answer was in the negative. And now Professor Wilson, speaking of later years, queried, "Why, in Belfast, has the disease been comparatively rare in spite of the large numbers of chronic carriers which must exist in the population?" If they could only accept the view that the bacillus was merely an "associated organism," they would cease to wonder why bacillus carriers, when studied on the grand scale (as in Belfast), should turn out to be as harmless as appeared to be the case.

Sir GEORGE BUCHANAN referred to the continued high mortality from enteric fever which characterized certain countries like France and the Balkan States, and particularly Japan. The continued high prevalence was practically explicable by the circumstances of the countries, and it seemed to cast doubt on the validity of the thesis which Dr. Wilson had tentatively put forward regarding the cause of the disappearance of typhoid in Belfast. If that disappearance had been due, in any substantial measure, to the exhaustion of susceptible material, one would expect to find similar results in heavily affected foreign countries, and also to have found the same disappearance in the past in those English towns which, in the days of privy-middens, presented so high an incidence of enteric year after year. He was particularly glad to know of the appreciation which had been shown to the work of Dr. Darra Mair, whose early death had been so great a loss to his department. Dr. Mair was a practical epidemiologist of much learning and sound judgment, and no one would have understood more than Dr. Mair himself the fact that explanations of an epidemic which he had given twenty years ago were now being reconsidered in the light of subsequent happenings. Whilst realizing the importance of these new facts, he (the speaker) doubted whether they led to any more plausible or probable solution of the problem of the occurrence of enteric fever in Belfast in 1898 than that which Dr. Mair propounded. This was, in a word, an explanation that a community which had the habit of consuming raw shellfish to an altogether exceptional degree, was, during the epidemic period, exposed to an exceptionally high risk of infection through the fact that the sewage contamination of the shellfish ordinarily eaten had definitely become more concentrated. In any case, the occurrence of that Belfast epidemic was one which was clearly the result of

exceptional circumstances, for which it seemed to him still likely that Dr. Mair's explanation was the true one.

In his opinion, the production of outbreaks by carriers, such as had been referred to in the paper, must be accepted as proved beyond dispute. At the same time, it seemed that the proportion of chronic carriers who were in a condition, or placed in circumstances, in which they could produce such infection as described, must be a very small one. He always felt a difficulty in explanations of past prevalence of enteric fever which depended on the supposition of unusual carrier infection. Thanks to various methods of sanitation, a stage seemed to have been reached in Northern Ireland, as well as in other parts of the United Kingdom, at which the number of cases and outbreaks of the enteric group had attained quite manageable proportions, and these cases and outbreaks could now be dealt with intensively and individually. By such concentration, and with the aid of the bacteriologist, we ought, before long, to secure that the annual figures of incidence and mortality from this group were reduced practically to vanishing point.

Dr. S. MONCKTON COPEMAN, F.R.S., said that Professor Wilson had set out very carefully the story of typhoid fever in Ireland, as compared with the concurrent experience of England and Wales and Scotland. The brief accounts of outbreaks of typhoid fever with which the paper ended afforded typical instances of the various ways, now well recognized, by which the disease might spread. He (the speaker) could well remember a time when, prior to appreciation of the part played in this matter by the healthy "carrier"—to mention one additional factor only—pollution of drinking water was universally regarded as the main cause for the spread of typhoid fever, as evidenced by the late Ernest Hart's tour of India for the promulgation, as he said, of the "gospel of the boiling kettle"! The further knowledge as to possible methods of infection that had accrued since that time had proved of the utmost value and assistance in the study of the epidemiology of typhoid fever.

In his appreciative summary of the work of the late Dr. Darra Mair, in connexion with investigation of continued prevalence of the disease at Belfast, Professor Wilson expressed some doubt as to whether the consumption of shellfish collected on the foreshore could have constituted a factor of such importance as suggested in the official report. He referred to the practical impossibility of preventing the collection and consumption of shellfish by private individuals, and evidently considered that the sedimentation and diversion of the sewage had played a specially important part in staying the progress of the disease. But it seemed to him (the speaker) that these two factors were not improbably inter-related. For it was known that shellfish were capable of ridding themselves of a certain amount of bacteriological impurity, and consequently the partial purification of the sewage brought about by the methods referred to might be expected to obviate, in large measure, the previously existing danger from consumption of the shellfish.

Dr. G. CLARK TROTTER referred to the opportunities Northern Ireland afforded for a wide range and suitable material. With regard to milk, in London, whilst a very small proportion of the total milk supply might be really true "raw" milk, practically the whole of the milk supply had been "treated" in some way. There was little opportunity for investigators to trace directly an isolated milk supply carrying infection, owing to the mixing in bulk and more or less efficient "pasteurization" which milk received to retard deterioration and conserve its quality. He could confirm what Professor Wilson had said about the difficulty of getting an indication of a probable cause in the diet; the relatives' statements were not as valuable as those of the patient. Recently, in a case he had seen, the relatives had omitted to state the fact obtained from the patient that she had partaken, within a fortnight, of periwinkles purchased off a street barrow. So also, the eating of fried fish—often imperfectly washed after gutting and not really sterilized by frying—was not thought of as a likely source of infection. He was a firm believer in the privy-midden of former days being a potent factor of infection; at the present day there was a tendency to think that the carrier cases, then unknown, would account for all infection. But the vast decline in enteric since the abolition of the privy-middens and introduction of the water-carriage system was too striking to be lightly set aside. Looking at Professor Wilson's charts of Northern Ireland, he would ascribe the marked decline to be due mainly to such improvements in sanitation.

Dr. E. W. GOODALL said that so far as this country was concerned the credit for the recognition of the importance of the typhoid "carrier" was due to Sir Percival Horton-Smith Hartley, who pointed out in his Goulstonian Lectures in 1900¹ that the stools and urine of

¹ *Lancet*, 1900, i, pp. 829, 830.

recovered patients contained the typhoid bacilli and might therefore in certain circumstances be the means of infecting other persons. In respect of the actual occurrence of such a method of infection he (Dr. Goodall) believed that the first instance was that recorded by the late Dr. Walker, of Peterborough, in the *British Medical Journal* of November 24, 1900.¹ It was a small outbreak, in which twelve persons contracted typhoid fever after drinking the water of a well at Long Orton, Hampshire, which had been contaminated, presumably, by the excreta of a soldier who had recently returned from South Africa after recovery from typhoid fever. Dr. Walker drew attention to the danger that might arise when so many soldiers, convalescent from typhoid fever contracted during the Boer War, were being invalided home.

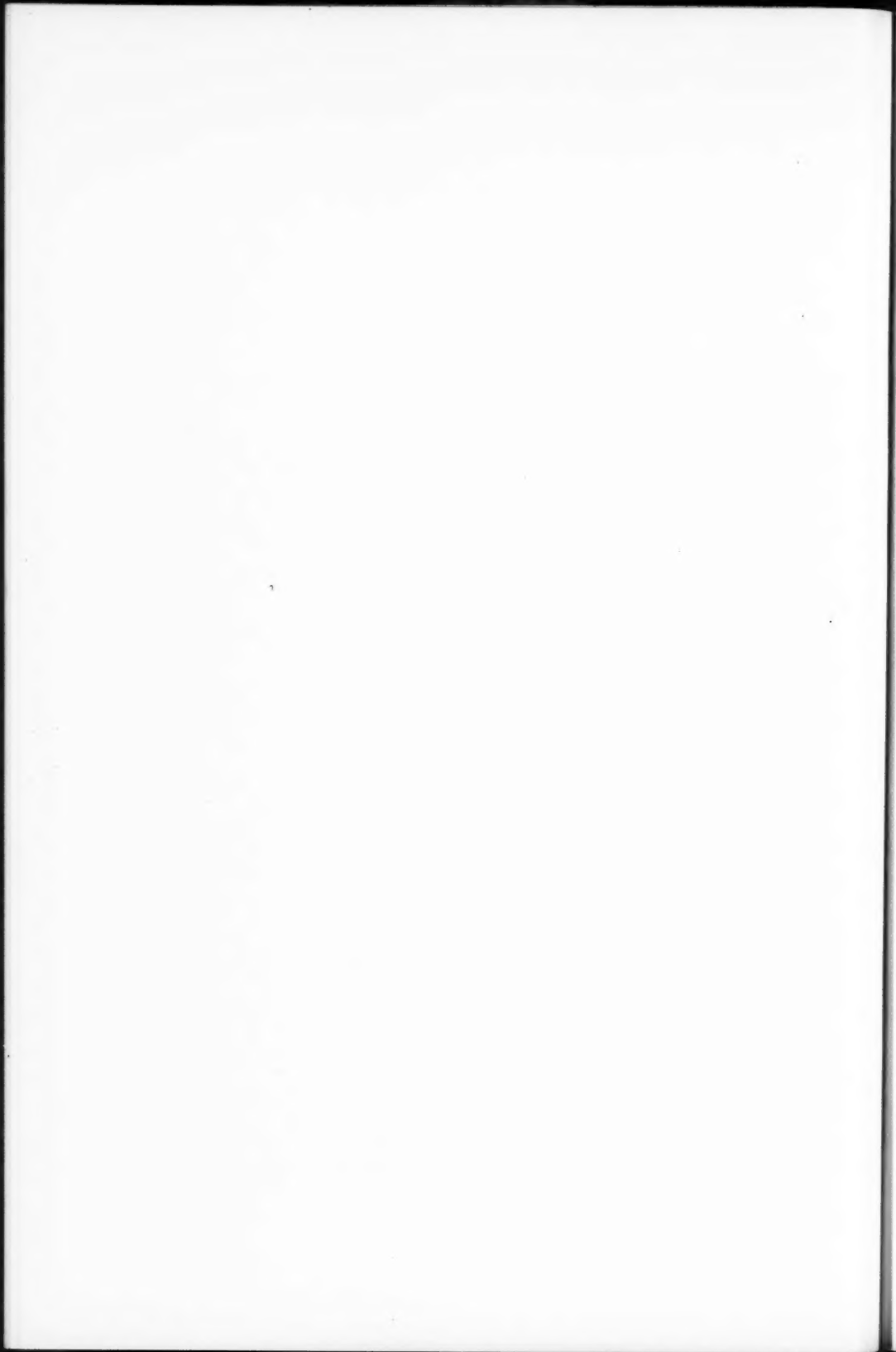
Professor WILSON (in reply) said he agreed with Sir William Hamer that the conditions under which the typhoid bacillus in the bodies of "carriers" became infective was still obscure. Probably several factors required to co-operate for this purpose. In the case of the *Bacillus typhosus* we had no virulence test and no susceptibility test such as we had for the *Bacillus diphtheriae*.

The epidemiologist and the bacteriologist should co-operate in an endeavour to throw light on many obscure problems in connexion with epidemic diseases. It was probably an advantage to the public health that the epidemiological study of enteric fever preceded bacteriological investigations and discoveries, as the epidemiologists laid such great stress on a clean environment, pure water supplies, &c., and the efforts to secure these desiderata conduced to the improvement of health in general. There might have been a temptation for bacteriologists to stress the specific nature of the infective agent and to direct their efforts against this alone, and perhaps to rely on active immunization.

To the work of Dr. Darra Mair the city of Belfast owed a deep debt of gratitude for his masterly epidemiological investigations, which stimulated and gave direction to subsequent sanitary efforts, resulting in the city ceasing to be a bye-word in the Kingdom as regards its enteric mortality. It was impossible to be certain as to the cause of the high mortality from enteric fever which Belfast had experienced; no doubt Dr. Darra Mair's shellfish hypothesis accorded best with the facts, but in his (Professor Wilson's) opinion only a small proportion of the enteric fever cases in subsequent years were caused by such consumption.

He (Professor Wilson) said he need not deal individually with the points raised by the various speakers—in many cases they had answered each other.

¹ *Brit. Med. Journ.*, 1900, ii, p. 1494.



Section of Epidemiology and State Medicine.

President—Dr. JOHN C. McVAIL.

The Conditions Influencing the Incidence and Spread of Cholera in India.

By Sir LEONARD ROGERS, M.D., F.R.C.P., F.R.C.S., F.R.S.,
I.M.S. (Ret.).

AT the present time the medical profession is generally agreed that the essential cause of cholera infection is Koch's comma bacillus, and that the disease is spread from place to place by human intercourse. There are, nevertheless, many facts regarding the incidence and spread of cholera in India that cannot be explained in the light of our present knowledge of the subject. These facts to some extent justified the long delay in the acceptance of the modern views regarding this serious epidemic disease, and formed the basis of the wind-extension theory, the last vestige of which was not removed until the 1894 edition of the Indian Army medical regulations was withdrawn. In these regulations the troops were ordered, when attacked by cholera, to march at right angles to the wind, and the edition was withdrawn as the result of the ridicule poured on it by Ernest Hart at the opening meeting of the first Indian Medical Congress held at Christmas of that year, at which I was present. Thus, the most striking argument of those who denied the infectivity of cholera, and the possibility of its being carried from place to place by human intercourse, was the undoubted fact, largely true to the present day, that cholera does not spread over India during the frequent epidemics any more rapidly in the era of rapid railway communications than during the first great epidemic of which we have any accurate data, 1817-18; that early epidemic, according to the great Madras authority, W. R. Cornish, having spread over the South of India to Ceylon considerably more rapidly than any of the outbreaks of 1859-1871 which he studied carefully. To the present day the regular sequence of events in Northern India is for cholera to become very prevalent in Eastern Bengal in November and December, in Bihar and the Eastern sub-Himalayan divisions of the United Provinces in March, the Southern and the Western United Provinces in April, and the Punjab not until May, in spite of railway communications uniting the extremes of this immense area in three days. Much the same is true of the relationship of cholera in Bengal and the Central Provinces and the Deccan divisions of Bombay.

The frequent epidemic exacerbations of the disease in various parts of India, its complete disappearance for a year or two at a time in large areas of the Punjab, the Central Provinces, and in the Sind, Gujerat and Deccan divisions of the Bombay Presidency, in spite of daily railway communication with the endemic areas, only to be followed by further serious epidemics in these areas without any material change from year to year in the appalling insanitary conditions of the vast majority of the population living in the villages—these facts all await explanation. It seems clear that until these riddles are solved little can be done beyond the exceedingly slow general improvement in sanitation, which, in such a poor country as India, as a whole, will require centuries to accomplish to the degree necessary for the prevention of cholera.

Yet another powerful, and at present unanswerable, argument of the anti-infectionist of India is that although the Hurdwar pilgrims by no means rarely

carry cholera broadcast over the Punjab from late in March or in April, the disease nevertheless dies down or remains latent until May or June, and then bursts out over such extensive areas simultaneously as to put out of court human intercourse as the sole agency in lighting up the epidemic. As that great Indian Medical Service statistician, James L. Bryden, pointed out in 1869—and the elaborate data he recorded over a series of years of the incidence of cholera among the troops and in the jails, the only figures then available, clearly indicated it—the Punjab epidemics coincided with the spread of the south-west monsoon current over that area, the earlier March and April “forerunner” cases as he calls them not producing epidemic cholera in these months. There was thus furnished a strong basis for the wind-borne theory of the causation of such epidemics, in the absence, at that time, of any knowledge of the causative organism, which was advocated as far back as 1820, by James Jamieson, in his most interesting and cautious account of the great epidemic of 1817-19 in the Bengal Presidency.

Yet again, it has frequently been pointed out that cholera does not increase first in the southern divisions of the United Provinces in most direct railway communication with the endemic areas in Bengal, but in the sub-Himalayan north-eastern divisions of that province, in which railway communications are of later and less advanced development; and other similar instances could be given.

Enough has been said to prove that we still have a great deal to learn regarding the factors which influence the incidence and spread of cholera over India, the solution of which may well lead to the establishment of a sounder method of controlling to some extent its ravages in India, where, in the decade 1812-21, it caused an average of 375,000 deaths yearly; and of obviating the possibility of its spreading by the usual overland route through Afghanistan to south Russia, which has certainly not been diminished by the present political conditions in south-west Asia and eastern Europe. Fortunately for nearly fifty years records of the monthly prevalence of cholera in all the districts of British-governed India have been reported in the voluminous sanitary reports of the different provinces and of Sanitary Commissioner with the Government of India. But no one seems to have been able to spare time from compiling these extensive records to make any use of the data for studying the all-important problem of cholera in India as a whole since the days of Bryden and Cornish over half a century ago. The problem of cholera in India has long interested me. During my residence in India I was able to find time to study its treatment, but, thanks to being superannuated while still not without some remaining energy, I have been able to devote many hours a day for most days of the week during the last twelve months to researches on the epidemiology of the disease, with results which I am sanguine enough to believe to be of considerable interest and practical importance. Before describing these it will be well to give a brief account of the observations and views of Bryden and Cornish, on which the still prevalent idea that cholera spreads over India almost entirely from Bengal appears to be mainly based, and to trace the spread of the 1817-19 epidemic.

THE SPREAD OF CHOLERA IN INDIA IN FORMER EPIDEMICS.

Before describing my own results from the study of the vital statistics of the civil population of India, it will be advisable to recall very briefly those of earlier writers on the subject, as a considerable change in some respects appears to have taken place in recent years, especially regarding the endemic areas of cholera. Strange to say, the most definite data on record for India as a whole, on the spread of an epidemic of cholera over this vast area, are those of the first great outbreak of 1817 to 1819, thanks to steps having been taken at once to collect all the facts by a questionnaire issued to every service medical officer in India by the medical boards of the three Presidencies of Bengal, including all northern and central India, Bombay and Madras. The medical officers of those days appear to have been

allowed far greater administrative powers under the East India Company than has ever been permitted by the Indian Civil Service in later years. The ostrich-like attitude of the Government of India may be judged from an illuminating remark in an old provincial sanitary report to the effect that the Sanitary Commissioner was prohibited by the Government of India officer from recording in his annual reports any details regarding the spread of cholera by infection or human intercourse. Fortunately, in spite of this prohibition, much scattered information bearing on the provincial spread of cholera is on record in some of the reports preceding 1900, when, under the late Lord Curzon's orders, the sanitary reports were so greatly restricted in size as to become little more than tables of figures, with too brief routine comments to be of much value. The data themselves, nevertheless, allow of much information being gleaned from them by patient work, as will appear in the course of this paper, and it is very strange that no such use has hitherto been made of them.

THE 1817-19 CHOLERA EPIDEMIC.

The spread of this great outbreak over northern and central India is admirably described by James Jameson in his book of 1820, which is favourably distinguished from most other works on cholera in India by containing a maximum of carefully collected facts, and a minimum of vain theorizing in the absence of any real



MAP I.—Spread of cholera in 1817-19 epidemic.

knowledge of the aetiology of the disease. A map of the spread of the epidemic over the Bombay and Madras Presidencies was made out by Scott, which was reproduced in W. R. Cornish's 1871 report on Cholera in Southern India; the data from both sources having been combined by me, I believe for the first time, in Map I. A brief description of this will suffice to bring out the main features of this remarkable epidemic, as the dates of the first appearance in a number of places, and arrows showing the direction of spread entered in the map largely speak for themselves.

It has frequently been asserted that this epidemic arose from a severe outbreak in Jessore to the north-east of Calcutta in August, 1817, but Jameson clearly shows

that cholera was endemic every year in the Bengal Presidency, and in August and September of that year it was epidemic throughout the province from Sylhet in South Assam through Eastern Bengal to the Bhagulpore division of Western Bengal. It spread further west to Patna and in November severely attacked the Marquis of Hastings' army to the south of the Jumna river in what is now the United Provinces. This attack was only shaken off after he had marched his army fifty miles across country to another river. The disease then subsided and ceased to spread during the cold season, as it always does to the present day in Bihar and the United Provinces for reasons not hitherto understood, but which I shall explain presently.

In 1818 cholera again became epidemic in the United Provinces at Allahabad and Banda in March, the usual month of increase in this area, and spread in several directions during the ensuing two hot weather months of April and May. Thus, the disease travelled west to the sub-Himalayan divisions of the United Provinces from Gorrahpur through Fyzabad to Lucknow and Rohilkund, as nearly always occurs to this day in that area: to the north-west through Cawnpore and Agra to reach Delhi, Saharanpur and Hissar in the Punjab during the rainy season months of July to September, which is as far as cholera extended this year in that direction. From Cuttack, in Orissa, on the west of the upper part of the Bay of Bengal, cholera spread down the coast to Gunjam in March, and Vizagapatam in May, but stopped there, as it still commonly does, being checked, as Cornish pointed out in 1871, by the sparsely inhabited hill tracts reaching down close to the coast at this point. From the northern area of the Central Provinces, invaded in April, the epidemic extended in two directions, first due south to reach Nagpur in May Secunderabad and Hyderabad in the centre of the Nizam's dominions in July, from whence a branch of the current passed to the central east coast districts of the Madras Presidency, attacking Ellore, Rajmundry and Masulipatam, in the densely peopled deltas of the Godavari and Kistna rivers in July, and another offshoot continued south to the north-central Madras districts of Cuddapar and Bellary in August and September. Meanwhile, from the Central Provinces the epidemic spread to the west in May to Bhopal, Ujjain and other Central India States, and to the south-east through Hoshangabad in May, to Nasirabad, Malegoan and Poona in the Northern Deccan in July, to reach Bombay and Dharwar in the Southern Deccan in August. It spread still further south to the west coast town of Mangalore in South Kanara in September, and in October and November most of the remainder of both coasts and central part of the southern peninsula was invaded, the extreme south to Palmacotta and Ceylon as well, being only reached in January of 1819.

I have traced the spread of this, probably the most terrible of all Indian cholera epidemics, at some length. It is not only the most carefully observed epidemic of all, but both Bryden and Cornish in their detailed accounts of subsequent epidemics up to 1870 regard that of 1817 as typical of the mode of spread of all such Indian cholera epidemics, especially as regards the extension of the disease. This extension was by what Bryden calls the northern epidemic highway, from Bengal through the United Provinces to the Punjab, and by his southern epidemic highway through the Central Provinces to the Deccan and other parts of the Bombay Presidency, and through Hyderabad to the Madras Presidency (see Map II). This round-about way through populated areas to reach Madras was the usual one in preference to spreading directly down the more sparsely populated east coast districts from Orissa. It is especially noteworthy that from the recrudescence of cholera in March, 1818, in the United Provinces the disease only took six months to overrun nearly all India, except the western Punjab, of which we then had little knowledge, and the southernmost part of the peninsula; the latter, as well as Ceylon, were reached within nine months. This was a more rapid spread than ever since met with, probably largely on account of the disease having been absent from the invaded areas for at least a number of years before 1817; but, nevertheless, it was

sufficient to prove that Bryden was right in holding that the greatly increased travelling facilities provided by improved roads, railways, and steamships, has not resulted in anything like a corresponding increase in the rapidity of the spread of cholera epidemics in India. This important fact still awaits a satisfactory explanation, which I hope to furnish later in this communication.

THE 1863-65 CHOLERA EPIDEMIC IN INDIA.

I next pass on to study the conditions of cholera spread in India sixty years ago, that is before regular vital statistics of the civil population of British-governed India were regularly recorded, but when accurate data had for some time been available of the incidence of the disease in the British and Indian armies, and in the numerous jails. Careful studies of this incidence were made with maps recorded by Bryden for northern and central India from 1854 to 1868, and by Cornish for the rest of India from 1859 to 1870. I have selected the 1863-65 epidemic as a typical one dealt with by both writers, and have combined their two complementary maps into one in my Map II, although only the areas invaded in each year can be shown for want of fuller data.

BRYDEN'S DATA FOR THE BENGAL PRESIDENCY.

Bryden shows the endemic area of perennial cholera (enclosed by thick vertical continuous lines in Map II) as including the western portion of Assam, all the deltaic region of Lower Bengal and Orissa up to the low Rajmahal and Cuttack hills to the west of this basin, but excluding Bihar, although he states cholera is always present



MAP II.—Spread of cholera in 1863-65 epidemic.

there, and he includes Eastern Bihar within the boundary line of his endemic area. To the north-west of his endemic area lies what he calls the "Eastern Epidemic Area," enclosed with broken lines in my Map II, and including Chota Nagpur, Western Bihar, and the eastern portion of the United Provinces up to Agra on its western border, also including Bundelkund to the south of the Jumna River. This area was invaded from Bengal, as shown by the army and jail returns, in 1863. According

to Bryden's maps and description, in those days cholera very rarely, if ever, spread beyond his eastern epidemic area in the first year of the progress of an epidemic from Lower Bengal over India. In the following year it might spread by his northern epidemic highway over the western portion of the United Provinces and the Punjab, or by his southern epidemic highway over the Central Provinces to the Deccan and Gujerat divisions of the Bombay Presidency. In 1864 he illustrates the invasion of this last area to the west and south of the dotted lines in Map II, but he does not deal with the peninsular portions of Bombay and Madras, which were outside the Bengal Presidency, with the figures of which alone he was concerned. I must, therefore, turn to Cornish's data to complete Map II, and first note a slight discrepancy between the two authorities. Bryden states that the Central Provinces and Bombay city were not invaded in 1863, but Cornish gives data of the infection of a track across the Central Provinces to the Bombay coast in June and July, 1863, which he remarks were thus invaded in the "teeth of the S.W. monsoon," in direct contradiction to Bryden's repeated and emphatic statement: "The assertion that cholera may advance against a prevailing wind is contrary to fact." Cornish further shows that in 1864 cholera spread over the whole of the peninsular portions of Bombay and Madras, with the exception of the Bellary district in Central Madras, the southern part of the portions of the east coast—all enclosed by dotted lines in Map II—which were, however, invaded in 1865, at the same time that a considerable portion of Bryden's Western Epidemic Area in north-west India—enclosed by a line of alternate dots and dashes in Map II—was attacked. He attributes the immunity of this area in 1864 to the repression of the disease by very dry famine conditions, although a possibly more likely explanation is that the Punjab had suffered from a severe cholera epidemic, as illustrated by other of Bryden's maps, in 1861 and 1862.

It is unnecessary at the present time to discuss Bryden's views on the spread of cholera, namely, that "the prevailing wind is the agency which directs the course of an advancing epidemic, and determines its limitation in geographical distribution," which is in accordance with Jameson's more guarded opinion regarding the 1817 epidemic, and is very similar to the conclusions arrived at in the 1856 report of Baily and Gull to the Royal College of Physicians of London. No one can read Bryden's careful study of all the available army and jail data without realizing that in the then prevailing state of ignorance of the nature and causation of the disease he was able to adduce strong arguments in favour of the wind-borne theory and against its spread by human intercourse. The facts supporting this theory were (1) the continued slow extension of cholera over the north of India in spite of much more rapid railway communications, and (2) the occurrence of cholera among pilgrims all over the Punjab after their return from the Hardwar fair late in March, or early in April, being followed by a tendency for it to die down, and not to result in any widespread epidemic before the monsoon set in about the middle of June. In connexion with this it is of great interest to note Bryden's further statements that "the conclusion is inevitable, that cholera, wherever met with, is entirely dependent on an atmosphere of moisture for epidemic invasion or progress," and again: "All these examples illustrate what I believe to be the universal truth, that it is with an atmosphere essentially humid that epidemic cholera is distributed." I shall show presently the basis of this assertion as regards India, which I have worked out with the help of meteorological data not available in Bryden's time, and quite independently of his conclusions. This I did before I had read his work.

Cornish, in his equally important contribution on the subject, showed that however strongly Bryden's wind-borne theory might be supported by the facts as regards northern India, in the case of the spread of epidemic cholera in South India: "The south-west winds do not stop or retard this southern advance, nor do the north-west winds hasten it." But he agrees that "the monsoon moisture has some

relationship to the seasonal intensity,"—an important fact which was emphasized and developed with regard to the Madras Presidency by Colonel W. G. King in his 1893 sanitary report for Madras. Unlike Bryden, Cornish recognized the great importance of pilgrimages in spreading cholera in India, and gives illustrative examples. He concludes that "it would be in the interests of the State, and of the people themselves, to prevent such assemblages in seasons of epidemic sickness."

The comprehensive inquiries of Bryden and Cornish showed that at the time they wrote all cholera epidemics appeared to originate in Lower Bengal at intervals of three or four years, and spread over nearly the whole of India in the course of some two years, recurring in the affected areas for two or three consecutive years, and then dying out again completely from whole provinces. Cornish concluded that "these epidemic waves of cholera recur at uncertain intervals, but generally once in four or five years." Some of them travelled through south-western Asia to reach Europe, as illustrated in maps in my book on cholera, now part of my "Bowel Diseases in the Tropics,"—a subject beyond the scope of the present paper.

CHOLERA CYCLES.

The question whether the recurring epidemics of cholera appear at sufficiently regular intervals to allow of their being foreseen has been the theme of much discussion in the past. The most striking contribution on this subject is H. W. Bellew's closely-printed "History of Cholera in India from 1862 to 1881" (800 pages), published in 1885, and supplemented by twenty years' statistics, printed in 1887, the greater part of which is devoted to maintaining that in every province in India cholera occurs in three-yearly periods of a very high prevalence in the first year and steadily decreasing ones in the second and third years. All the exceptions, which in Assam greatly exceeded the years following the rule, were ingeniously, but not very conclusively, explained as due to abnormal rainfall, prices of foods and other such constantly varying factors. During the past six years a six-year cholera cycle has been propounded by Major J. H. Russell, Sanitary Commissioner of Madras, in ignorance of the views of his numerous predecessors. But from a study of the tables I have worked out during the last twelve months of the cholera rates per mille for over 200 districts and forty-five divisions of India, for a period of forty-five years, I am unable to trace anything like a three-year, up to a six-year cycle if a long period of time is studied. I therefore agree with Cornish in his statement that Indian cholera epidemics occur at irregular intervals, the main causative factors of which will appear later in this paper.

It is also of interest to note that only about a year ago Lieutenant-Colonel Fry, Sanitary Commissioner of Bengal, from a brief study of the number of thousands of cholera deaths per year in different Indian provinces, concluded that the views I have shown above to have been advocated by Bryden and Cornish regarding the origin of Indian epidemic cholera from Bengal still hold good, a question I shall deal with presently in the light of my prolonged study of the records since Bryden's day.

I do not propose to discuss the extreme anti-infectionist views expressed by Surgeon-General J. M. Cunningham, not because I fear to share the fate of Andrew Duncan, one of the ablest I.M.S. officers of his day, whose career in India was absolutely ruined for daring to write a paper including views contrary to J. M. Cunningham's ardently held wind-borne theory of its spread, published in 1884 after the discovery of the cholera vibrio; but because the perusal of his work, taken with the orders issued in his time, forbidding the publication of views regarding cholera being spread by human intercourse, as already noted, convince me that the most charitable view to take of his action and writings is that he considered it his duty to support in every way possible the political views of the Government of India, whom he served so long and faithfully as their Sanitary Commissioner.

THE STATISTICAL DATA OF THE FORTY-FIVE YEARS ANALYSED.

The mortality figures of the civil population began to be recorded for some provinces in 1865, but unfortunately, owing to the backwardness of Bengal, the home of cholera, it is only since 1877 that the monthly data have been available for each district of British-governed provinces of India. I have tabulated these figures for the 206 districts for forty-five years from that date, and also worked out the annual rates per mille for each division, comprised of three or more districts, as well as the months in which the disease appeared or became more prevalent, and those of maximum incidence for the forty-five divisions. Almost every figure has had to be worked out from the published data, for although every province except Madras arranges the district figures in geographical divisions, scarcely any of the reports give the divisional figures themselves. As in several provinces the arrangement of the districts in divisions has been changed from time to time, this necessitated the preparation of tables of the districts year by year, arranged in the present divisions. The annual rainfalls have also been studied for every province and for several of the divisions, and innumerable charts worked out, the whole investigation having taken over a year of hard work. In addition, I have typed out the most important information on cholera in the sanitary reports for all India, as well as in many of the provincial reports, so that the results of my investigation now to be dealt with are based on a very comprehensive study. Cholera is such an easily recognized disease when the cases are present in any numbers that the data afford reliable evidence of the variations in different areas from year to year, especially as the cholera death-rates in any of the epidemic areas commonly vary from one year to the next by a ten to a hundredfold or even to a thousandfold difference, which renders imperfections of the yearly variations in reporting the deaths of little or no moment for the purposes of this inquiry.

AVERAGE PROVINCIAL AND DIVISIONAL MONTHLY VARIATIONS IN CHOLERA MORTALITY.

The first requisite is to obtain clear ideas regarding the very variable monthly distribution of cholera in different parts of India; to illustrate these the data of fifteen years' average figures of those provinces presenting fairly homogeneous areas from this point of view, and for ten years of certain other areas selected for similar reasons, together with the principal meteorological data in the same months, are all plotted out in Diagram I, on similar lines to those of my recent study of small-pox in India, which gave me the clue to the relationship of that disease to absolute humidity. Maps III and VI also give the average cholera mortality for the same areas for the main seasons of the year, the whole furnishing full data for studying this important aspect of the subject, which may now be discussed in the light of Diagram I and the maps. As a matter of fact, I have worked out similar data for twenty-one divisions, but the eight selected will suffice to bring out all the important types, and the maps show the seasonal incidence of cholera for all British provinces arranged in twenty-one areas, and enable each to be studied, although only the selected ones can be discussed in any detail.

From the monthly mortality figures for the whole of India for eight years, given in a table in Bellew's "History of Cholera in India" 1885, and confirmed by later experience, it will be seen that the minimum mortality occurs in October and November. But there is a considerable rise in December, due solely to a great increase in Assam, Lower Bengal, and in Central and South-east Madras, for in the whole of the rest of Northern and Central India the disease falls greatly to its minimum during the cold weather months, and it is especially noteworthy that the Lower Bengal and Assam rise commences in October and November immediately after the cessation of the south-west monsoon rains. During the prevalence of these this area is mostly under water, and cholera is at its minimum here just when

its maximum occurs in most of India, as shown in Map V. Proceeding north-west from Lower Bengal we find the next increase in March in Bihar and Chota Nagpur, which formed the western part of the Bengal Province up to 1911; in April a great rise occurs in the United Provinces and in the Central Provinces further west, although the increase commences in the Central Provinces and the Deccan in March, while the increase is not marked in the Punjab until May, and in recent times nearly always in the same year as in the United Provinces. It should, however, be noted that in the north-eastern sub-Himalayan portion of the United Provinces immediately to the west of Bihar, the rise begins a little earlier than in the divisions bordering on the Punjab, a gradual shading off in the rate of increase occurring in this extensive province from east to west. All this at first sight supports the generally accepted view that the home of cholera is in Lower Bengal, from which it spreads steadily month by month to the Central and United Provinces and on to the Punjab. On examining the cholera maps of the Bengal and other provincial reports, which unfortunately were omitted under the orders of the Government of India in 1900, I found that whenever cholera was in excess in any year in Bihar, it always also increased in the United Provinces, as in 1892 and 1894, and often later in the Punjab. When it was most prevalent in the southern Orissa division of Bengal it also increased a little later in the neighbouring eastern divisions of the Central Provinces, while if it was only markedly prevalent in Eastern Bengal it was also high at the same time in Assam, but was not so prevalent in the areas to the west of Bengal; all these are facts supporting the ideas prevalent for over a century, the truth of which at this stage of my investigation I was fully convinced. I had long ago noticed, while working at the treatment of cholera in Calcutta, that in epidemic years we had many more admissions than usual in November and December, after the monsoon quiescent period, and I hoped that by watching the rise in those months an epidemic might be foreseen before it spread beyond Bengal, with the possibility of taking certain precautionary measures against its extension.

A peculiar and significant feature in the Assam and Lower Bengal curves remains to be noted, namely, that the October to December rise is followed by a remarkable fall in January, still further accentuated in February, but succeeded by a second rise in the hot-weather months of March to May, synchronizing with the rise in the more westerly provinces of Central and United Provinces. The relationship of the seasonal incidence of cholera in relation to certain physical phenomena was studied by T. R. Lewis and D. D. Cunningham in their paper of 1878, from which they concluded that cholera was a soil-borne disease like malaria. They contrasted the meteorological conditions and cholera incidence in Calcutta and Lahore, and attributed the very low cold-weather rates in the Punjab to the low winter temperatures, and also pointed out that the relative humidity at the time of the maximum Lahore prevalence was not much removed from that of Calcutta during the second rise in March and April. We may now study this point further with the advantage of the data of the Indian "Atlas of Climatology," published in 1906, including the absolute humidity data shown in Diagram I and Maps III to VI.

CLIMATE AND CHOLERA INCIDENCE IN INDIA.

Diagram I gives for each of the eight selected areas the monthly rainfall and the mean monthly absolute and relative humidities in the lower halves; and the monthly cholera per 100,000 and mean monthly temperatures in the upper portions. The rainfall alone clearly will not explain the seasonal distribution of cholera in India as a whole, for the disease is at its minimum during the south-west monsoon in Assam and Lower Bengal, but at its maximum at the same season in the Punjab, the Deccan area of Bombay and the Central Provinces. The mean temperature certainly shows a closer relationship in so far that the disease is at its minimum during the winter season in the colder Punjab, United and Central Provinces and

Deccan, but in Lower Bengal it will be observed that the lowest cold weather month is February, when the temperature has begun to rise. Once more the relative humidity, in the Punjab for example, is nearly as high in the minimum cholera months of December to February as in the maximum ones of the rainy season in July. There only remains the absolute humidity or aqueous vapour pressure, which is measured as air pressure in terms of the length of a column of pure mercury at temperature 32° , and is obtained from observations of the wet and dry bulb thermometers by means of special tables prepared with August's formula modified by Regnault, as described by Sir John Elliot in the atlas already referred to. Here, once more, we find no relationship between a high absolute humidity and cholera

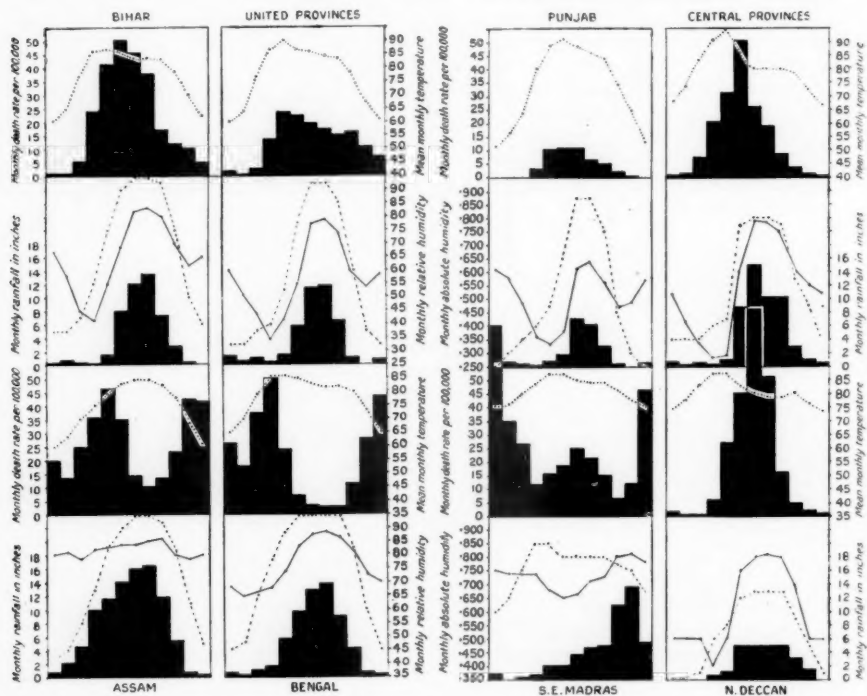


DIAGRAM I.—Cholera and climate in India.

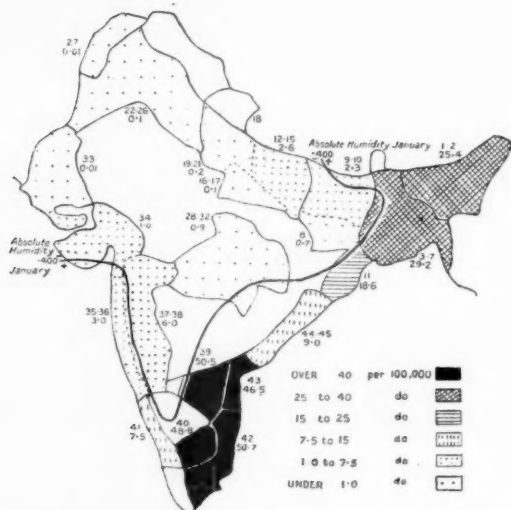
incidence, but when we turn to the months of low absolute humidity we find that in every area in which this reading falls below 0.400 during the cold weather months, cholera at the same period falls to a very low rate, as in Bihar, the United Provinces, Central Provinces and North Deccan, and altogether disappears as in the Punjab. Still more significant is the fact that the winter decline of cholera in Assam and Lower Bengal in January and February immediately follows the lowest absolute humidity in December to February of from 0.425 to 0.475, and the mortality rises once more in these areas with the much-increased absolute humidity in March, so that this factor is sufficient to explain the slight Assam and Bengal winter fall, as well as the greater ones in the colder provinces. Equally close is the relationship to

increasing cholera prevalence in North-western and Central India, for the marked cholera rise in the Central Provinces and the United Provinces occurs in April when humidity reaches 0'400 or above, and in the Punjab it is delayed until May with a later rise in the humidity above the critical point, as will appear more clearly when we consider Maps III to VI.

The autumn decline to the minimum in November and December in the same areas also coincides with a fall of the absolute humidity to below 0'400, completing the evidence of the closest association with that degree of dryness and falling cholera mortality, and indicating that this condition is unfavourable to the continued survival of the infective agent outside the human body in sufficient quantity to keep up the epidemic prevalence of cholera over large tracts of country. As the absolute humidity is essentially a measure of combined temperature and moisture, it is not surprising that these conditions affect extra-corporeally the life of the cholera vibrio, for it is certain that during severe epidemics in India the organism becomes very widely distributed in the infected area. A century of military experience has shown that the only effective way to shake off the disease from a body of infected troops is to move them away from the place in which they are suffering, as the Marquis of Hastings did so effectually in Bundelkund in 1817; the experience of this measure in the case of infected famine relief works and jails is precisely similar.

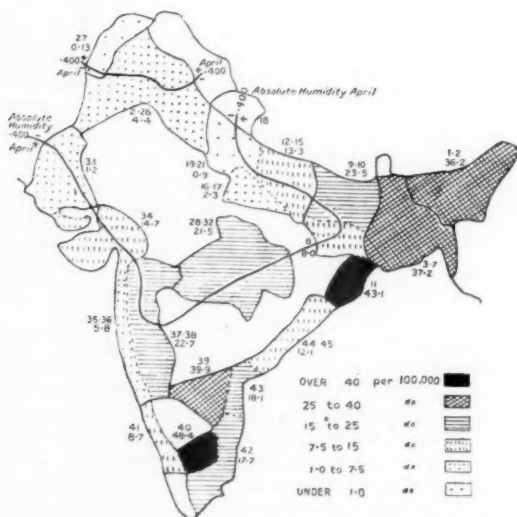
SEASONAL INCIDENCE OF CHOLERA IN INDIA.

In the light of the foregoing climatic influence the maps of the seasonal incidence of cholera in various parts of India will only require a brief description, commencing with the minimum season for most provinces of the cold weather months of December to February illustrated by Map III, in which I have inserted the January 0'400 absolute humidity line, areas to the east and south of it having a higher, and to the north-west a lower reading. It will be seen at a glance that all the areas with a high average cholera rate in this season, namely, Assam, Lower Bengal, Orissa, South Central and East Madras, all lie within the smaller area, with a minimum absolute humidity of over 0'400, and all the areas of minimum low cold weather cholera incidence have an absolute humidity below that critical point. Passing on to Map IV, showing similar data for the hot season of March to May, in which I have inserted the April 0'400 mean absolute humidity lines, it will be seen that the high cold weather cholera areas above-mentioned still maintain high rates, and that the incidence of the disease has now increased considerably in Bihar (3), the sub-Himalayan north-eastern Gorraekpur, Fyzabad and Lucknow divisions of the United Provinces (5); that is, just the areas where the absolute humidity has risen to over 0'400—the March line being almost the same as the April one shown—as well as in the Central Provinces and the Deccan, through which the critical line runs. The district data show that the rise takes place earlier in the eastern part of the Central Provinces where the humidity first increases. Once more the lowest rates occur in the south-west divisions of the United Provinces, North-West Frontier, the Punjab and Sind, precisely the areas in which the absolute humidity in part or the whole is still below 0'400, the Konkan (15) or west coast of Bombay, with poor communications for the most part and little cholera, is the only low area with a higher humidity. In May the only area with an absolute humidity below 0'400 is a very minute oval one in Central India. When we pass on to the Map V of the rainy season incidence from June to September, we arrive at the period of highest yearly absolute humidity, when the lowest reading is 0'650 and the highest 0'950. It is in this season that cholera reaches its maximum in the whole of India outside Assam, Lower Bengal, Orissa and South-east Madras, that is, the areas with no great cold weather remission of the disease, for cholera very rarely maintains a continuous very high incidence for more than four or five months in the epidemic

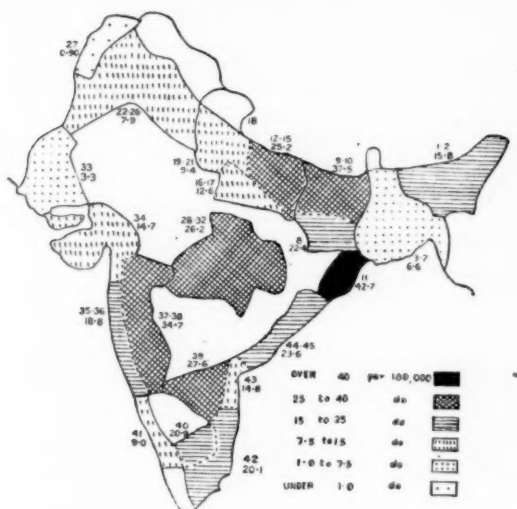


MAP III.—Average monthly cholera per 100,000, December-February.

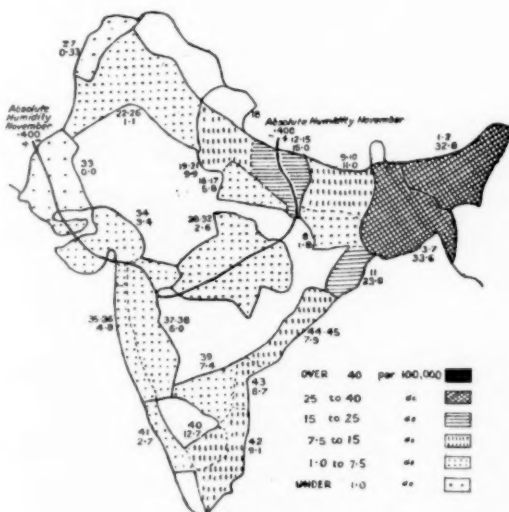
1-2, Aesam. 3-7, Lower Bengal. 8-11, Bihar and Orissa. 12-21, United Provinces. 22-26, Punjab. 27, N.W. Frontier Province. 28-32, Central Provinces. 33-34, Sind and Gujarat. 35-36, Bombay Coast. 37-38, Bombay Deccan. 39-40, Central Madras. 41, Malabar Coast. 42-45, East Coast, Madras.



MAP IV.—Average monthly cholera per 100,000, March-May.



MAP V.—Average monthly cholera per 100,000, June-September.



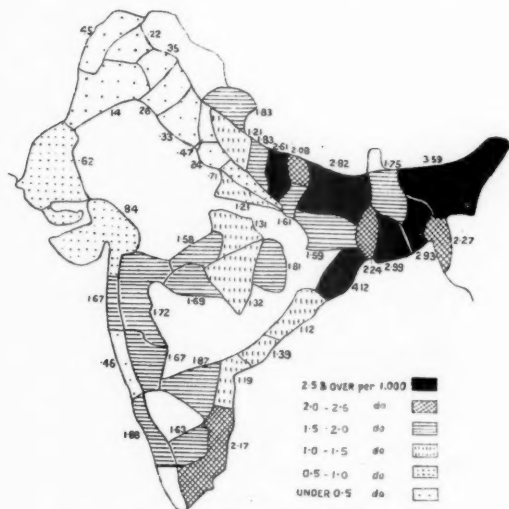
MAP VI.—Average monthly cholera per 100,000, October-November.

areas. Yet this is the very time of the year when cholera falls to its lowest point in the deltaic region of Lower Bengal, when most of the country is flooded and the water supplies are flushed out and cleansed by the abundant rains, and the vast volumes flowing down the mighty Ganges and Brahmaputra rivers. There only remains the period of decline in all parts of India except Lower Bengal and Assam, shown in Map VI, especially in October and November; during November the area of humidity below 0'400 spreads from a small area in the extreme north-west corner of India in October to include all the Punjab, where the decline is first pronounced, all but the eastern border of the United Provinces, the north-west half of the Central Provinces, and the dryer inland parts of Sind and Gujerat, as shown in Map VI. But this decline is accompanied by a great rise in damp Assam and Lower Bengal, where even the November absolute humidity is still over 0'550.

This extremely close, but as far as I am aware hitherto unrecognized, relationship between cholera incidence and absolute humidity all over India opens up the all-important question as to how far the later seasonal rise of cholera incidence in Bihar and the greater part of the United Provinces—in short, Bryden's "Eastern Epidemic Area"—is due to the inhibition of the disease by low humidity in the winter season, and not to the spread of cholera from Lower Bengal, as has up to now been believed.

THE ENDEMIC AND EPIDEMIC AREAS OF CHOLERA IN INDIA.

The real question is essentially to map out the endemic areas of cholera in India. For this purpose sufficient data did not exist in the time of the earlier writers, to whom I have already referred, but the forty-five years' records of forty-five divisions



MAP VII.—Average annual cholera per 1,000.

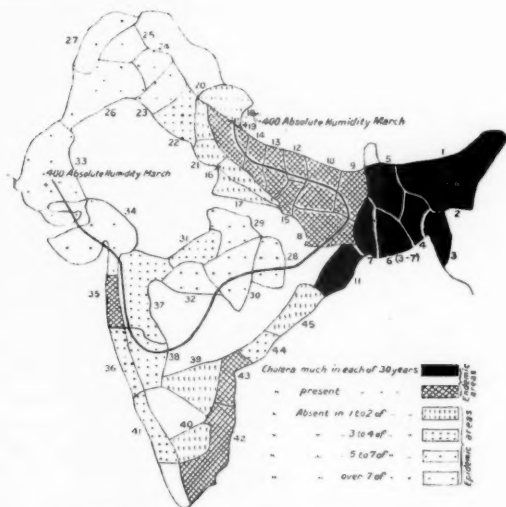
of India in my tables now furnish material for determining these areas. In this connexion Map VII of the total annual average rates per mille, derived from the data of thirty years up to 1919, may first be considered. It will be observed that the highest rates of 2'50 per mille and over, represented by the uniform dark shading in

the map, include the Brahmaputra and Surma Valleys of Assam, the Dacca and Presidency delta divisions of Lower Bengal, Orissa, the easterly Bhagulpore, and the westerly Patna division of Bihar, the latter including the later formed Tirhoot division, and the Fyzabad division of the sub-Himalayan area of the United Provinces. The next highest incidence of from 2'00 to 2'50 includes the Chittagong and Burdwan divisions of Bengal, the Gorrackpur area of the United Provinces and the large and densely populated low-lying and greatly irrigated districts of South-east Madras from South Arcot in the north to Tinnevely in the extreme south of the peninsula. All except the Bihar and United Provinces divisions have an absolute humidity of over 0'400 throughout the year, while the latter areas are the first in which that degree is reached in March and continues to November. At the other extreme, with the lowest annual cholera rates, we have the most westerly Agra and Meerut divisions of the United Provinces and the whole of the Punjab, comprising Bryden's "Western Epidemic Area," Sind and Gujerat,—all dry areas. It is also noteworthy that the Jubbulpore and Nagpur divisions of the Mid-Central Provinces have lower rates than easterly Chattisgarh or the westerly Nerbudda and Berar divisions, while the north-east coast of the Madras Presidency, between the high incidence area of Orissa to the North and South-East Madras, also has a comparatively low rate. It thus appears that the most essential factor in producing a high annual cholera-rate is the absence of any lengthy period of absolute humidity sufficiently low to greatly check or completely inhibit the prevalence of the disease; this factor may also influence the extent of the endemic area.

THE PRESENT ENDEMIC AREAS.

To determine the present endemic areas we require to know the divisions in which cholera is never absent over a considerable series of years. Map VI has been prepared to illustrate this, as well as the frequency with which the disease has been entirely absent for a whole year at a time. In studying my tables from this point of view, I found that Lower Bengal, Orissa, and Assam differed from all other areas in India in showing very small variations from the average incidence from year to year, which can best be defined by the statement that in this area of contiguous divisions, showed as uniformly darkly shaded in Map VIII, the annual rate per mille never fell as low as one-tenth of the average figure of the thirty years under consideration. This region may conveniently be called the hyperendemic cholera area, and it will be noted that it has an absolute humidity of over 0'400 throughout the year, in common with the south-eastern portion of the peninsula. The remaining divisions in which cholera has been present in every one of the thirty years' continuous records are shaded by crossed lines in Map VIII, and include: (1) the extra-deltaic western divisions of Bengal, namely, Bihar and Chota Nagpur, and the north-easterly sub-Himalayan divisions of the United Provinces, namely, Gorrackpur and Benares, immediately to the west of Bihar and Chota Nagpur, and the Fyzabad, Lucknow, Rohilkund divisions, in that order, from east to west, stretching up to the south of the mighty range of the Himalaya Mountains (it will be observed that it is precisely in this tract of country that the absolute humidity rises in March to over 0'400); (2) the extensive low-lying alluvial districts of South-east Madras, between the low Eastern Ghat Mountains and central plateau and the west coast of the Bay of Bengal; (3) a small low-lying strip of the North Konkan districts of Bombay between the abruptly rising Western Ghat Mountains and the west coast; the last two also having an absolute humidity of over 0'400 throughout the year, while, as a rule, in these areas cholera was present in every month of the year during the last two or three decades. Endemic areas therefore now exist in each of the three presidencies, whatever may have been the case sixty years ago, when Bryden limited the endemic area to Lower Bengal and Western Assam, and Cornish considered the disease not to be endemic in Madras. The latter opinion was supported by the almost complete absence of cholera

from south-east Madras in 1874 and 1880, both years of very low cholera incidence in India. It should also be noted that Bryden stated that cholera was never entirely absent from his Eastern Epidemic Area in the period he studied, although it became very greatly reduced in the years preceding the apparent new spread of the epidemic disease from Bengal. It thus appears that in the Madras Presidency, at any rate, the endemic area of cholera has considerably extended during the last few decades, and Major A. J. H. Russell, Director of Public Health, Madras Presidency, informs me that he has independently come to the conclusion that South-east Madras must now be considered to be an important endemic area of cholera, from whence it spreads to the surrounding areas.



MAP VIII.—Cholera endemic and epidemic areas.

Divisions.—1, Assam Valley. 2, Surma Valley. 3-7, Lower Bengal. 8, Chota Nagpur. 9, Bhagulpur. 10, Patna and Tirhut. 11, Orissa. 12, Gorakhpur. 13, Fyzabad. 14, Lucknow. 15, Benares. 16, Allahabad. 17, Jhansi. 18, Kamaon. 19, Rohilkund. 20, Meerut. 21, Agra. 22, Umballa. 23, Jullunder. 24, Lahore. 25, Rawal Pindi. 26, Multan. 27, N.W. Frontier. 28, Chattisgarh. 29, Jubbulpore. 30, Nagpur. 31, Nerbudda. 32, Berar. 33, Sind. 34, Gujarat. 35, N. Konkan. 36, S. Konkan. 37, N. Deccan. 38, S. Deccan. 39, N. Central Madras. 40, S. Central Madras. 41, Malabar Coast. 42, S.E. Madras. 43, Central E. Coast. 44, Kistna and Godaveri. 45, Vizagapatam and Gunjam. *Lower Bengal.*—3, Chittagong. 4, Dacca. 5, Rajshahi. 6, Presidency. 7, Burdwan.

The endemic areas just dealt with differ from the hyperendemic area of Lower Bengal, Orissa and Assam, in that, although cholera is never absent for a whole year, yet the rate per mille not very rarely falls to less than one-tenth of the average rate. This appears to be due, in the case of western extra-deltaic Bengal and the north-west United Provinces, to the much greater decrease of cholera in the cold season with the fall of the absolute humidity to below 0'400 from December to February, and in the case of South-East Madras and the northern Konkan area of Bombay, to the conditions there being less favourable to cholera than the very low-lying delta of the Ganges and Brahmaputra rivers.

It should be mentioned at this point that I have taken a return of less than 0'01 per mille per annum for any district as an absence of cholera, for the reason that the

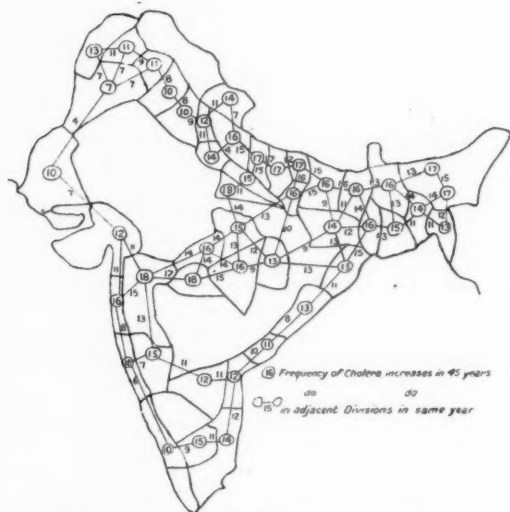
return by an uneducated village watchman of an isolated death or two from acute diarrhoea as cholera is no evidence that it was really due to cholera, as has recently been proved in the case of the Bengal coal-fields by the investigation on the spot, by Captain G. C. Maitra, I.M.S., of the Calcutta School of Tropical Medicine, that such isolated cases are rarely true cholera, and that when cholera is present there are almost invariably several deaths in a single village at about the same time. Isolated cases of diarrhoea, returned as cholera, not producing a mortality of 0·01 per mille per annum, have therefore been disregarded in discussing the incidence of the disease over a series of years.

THE EPIDEMIC AREAS OF CHOLERA.

Passing now to the divisions in which cholera has been absent for a year or more during the three recent decades under consideration, I have classified them in accordance with the number of years of absence in that period, and have shaded the divisions in Map VIII according to the scale noted in it. Absence during only one or two years out of the thirty is shown by short vertical lines. Those divisions with absence for three or four, five to seven years, and with over seven years respectively, are shown by dots at increasing intervals, so that the lightest shading corresponds with the lowest cholera incidence. The result is highly instructive, for it will be seen at a glance that the incidence in the south-west of the United Provinces and in Punjab divisions shades off uniformly with their increasing distance from the endemic areas of Bengal, Bihar and north-east United Provinces; and that the distant and dry divisions of Sind and Gujerat share with the equally dry Western Punjab in having the lowest cholera incidence in India. The elevated central plateau of India, comprising the Central Provinces and Deccan, with a much drier climate than Bengal and the coastal areas of Bombay and Madras, also have a low incidence, especially the Central Provinces and Berar, and this area has a low absolute humidity comparable to that of the Punjab during March and April. Once more, the Central Madras divisions, with a considerably greater elevation, lower rainfall and drier climate than the coastal areas of the peninsula, have a distinctly lower incidence than the humid east coast districts. In a word, the frequency of the absence of cholera from any area is in close relationship with the degree and duration of the very low absolute humidity of under 0·400 during the year; and it should be emphasized that this low degree indicates a very dry atmosphere, combined with a moderate temperature, slight variations from which can only be detected by hygrometric measurements, 0·400 being, in fact, less than half the minimum humidity even in the very dry Sind and Punjab during the incidence of the scanty rainfall of those areas during the south-west monsoons. So that these low readings do not occur during the hottest and driest portions of the year in Central and North-West India when cholera is often prevalent, which is doubtless the reason why their importance has not hitherto been realized. It is not too much to say the exceedingly close relationship between absolute humidity and the annual and seasonal incidence of cholera I have now demonstrated must be understood and continuously borne in mind in considering the causation of the great variations of epidemic cholera, and the incidence and spread of epidemic cholera from year to year, which still remains to be dealt with. The knowledge of the fact of this close relationship is also of the utmost practical importance in attempting to check the progress of such epidemics, as it furnishes the key to likelihood of cholera introduced by human agency becoming epidemic in any given place, and at any particular season of the year. Further, the yearly variations of absolute humidity must be examined with other meteorological data when studying the influence of climate as a whole on the occurrence and spread of epidemic cholera in India—a vast problem, of which there is only time to make a general survey in this paper.

FREQUENCY OF EPIDEMIC CHOLERA IN INDIAN DIVISIONS IN RELATION TO
NEIGHBOURING DIVISIONS.

I now pass on to study the yearly variations in cholera. For this purpose I plotted curves of the yearly rates per mille from 1877 to 1922 for forty-five divisions of India, the details of which it is obviously impossible to deal with as part of a single paper, so I next worked out the number of distinct yearly rises of cholera incidence in each division, and the frequency with which an increase occurred in the same years in contiguous divisions. I have entered the data in Map IX in order to show the general results of this lengthy inquiry almost at a glance. One or two points which cropped up in this part of my work require to be mentioned. In the first place I have already pointed out that in Assam and Lower Bengal the yearly rise of cholera begins in October to December, in South-East Madras the increase sometimes commences in December, but in other parts of India only during the hot weather months of March to May, on account of the varying absolute humidity



MAP IX.—Frequency of divisional cholera epidemics.

already so fully dealt with; further, the Lower Bengal cholera is at its minimum in the rainy season when the maximum is met with in Upper and Central India. If cholera epidemics always spread from Bengal, as hitherto thought, it is clear that the occurrence and degree of the exacerbations of cholera in that province must be calculated on the mortality from October one year to September of the next, and compared with those of other areas from January to December of the year following the October Bengal rise. Both in my tables, curves, and in Map IX, as well as in the yearly maps to be dealt with later, all the Bengal and Assam data have been recalculated on that basis. Another difficulty is due to cholera being sometimes high in two successive years in any given division owing to recrudescence in the second year of an epidemic commencing in the first year; these have been considered as one epidemic rise, and if in either of the two years there was a marked rise in the incidence in a neighbouring division, the two are considered to be related.

It should also be pointed out that the occurrence of cholera increase in two neighbouring divisions may be due, first to the same climatic or other conditions influencing the prevalence of the disease in both areas at the same time, or secondly, to the spread of the disease from one to the other. To decide on which is the more important factor it is necessary to know the dates of the increase in each division, but this aspect of the question must be considered later, and only the broad conclusions will now be indicated.

In the first place, if cholera epidemics still originate in Lower Bengal and spread over the whole of India in the course of a year or two, as was undoubtedly the case in 1817-18, and probably much later, the number of the exacerbations should be highest in Bengal and should tend to decrease with increasing distance from Bengal. This is clearly not the case, for although Assam showed seventeen rises in the forty-five years charted, the Lower Bengal deltaic divisions showed only fourteen to sixteen, Bihar sixteen; yet the three westerly sub-Himalayan divisions of the United Provinces show no less than seventeen rises, and Jhansi, the most southerly division, had eighteen. Still further to the north-west, in Bryden's westerly epidemic area, however, there is a well-marked decrease in the number of epidemics to ten and eleven in the sub-Himalayan divisions of the Punjab, to only seven in the very dry Mooltan division in the south-west of the Punjab, in calculating which it should be mentioned that only a rise of at least 0.1 per mille per annum was regarded as a definite increase. For in one or two other years a still smaller increase did occur in the Mooltan division, so the difference is rather one of degree than of kind, and is clearly once more related to the exceptionally low absolute humidity of that division, even for the dry Punjab. It will be recalled that cholera is frequently entirely absent from the Punjab for a year or two at a time, so here we have clear evidence that the epidemic invasions of the Punjab are considerably fewer than the rises of cholera in the endemic area to which I have drawn attention in the United Provinces. As it is also evident that fourteen to sixteen Lower Bengal epidemics cannot well give rise to seventeen in the United Provinces, these data confirm in a striking manner my conclusion from the data in Map VIII that cholera has, at any rate, been endemic in the sub-Himalayan tracts of the United Provinces for at least forty-five years, and probably for much longer. Still more conclusive evidence is obtainable from studies of maps of the yearly prevalence of the disease dealt with later.

The Central Provinces, including Berar, furnish a very interesting example of the value of this line of investigation, and throw light on the reason for the lower cholera incidence in the two middle divisions, and on the question how far cholera from Bengal still overruns the Central Provinces to reach the Deccan and Madras, as in the 1817 outbreak and several of those between 1856 and 1868 described by Bryden and Cornish. Beginning with the Chattisgarh easterly division of the Central Provinces, we find that in every one of the thirteen epidemic years there was also a rise in the Orissa division of South Bengal, which includes the great pilgrim centre of the famous Jaganath temple at Puri, the importance of which in spreading cholera in India has only been equalled by the apathy of the local governments in providing protective sanitary measures for the town. Moreover, in ten of the thirteen outbreaks in the Chattisgarh division, another great pilgrim centre at Benares also showed cholera rises. The northerly division of Jubbulpore had fifteen years of increased cholera, in no less than fourteen of which the neighbouring southerly Jhansi division of the United Provinces also showed enhanced rates, including some years when the rate was low in other parts of that province, so that the very high number of eighteen epidemics in the Jhansi division is clearly due to this division being invaded from the Central Provinces as well as from the endemic areas of the United Provinces themselves. The same remark applies to the sixteen outbreaks in the southerly Nagpur division of the Central Provinces, which other data also clearly show to be invaded in different years from either the easterly or the westerly

divisions of that province. Even more striking is the fact that in seventeen of the eighteen epidemic years in Berar, in the south-west of the Central Provinces, the North Deccan to the west was also involved, while the divisions to the north and east of Berar were only affected in sixteen years each. So here again it is clear that Berar must sometimes be invaded from the Bombay province to its west, as other records clearly show to be the case. We can now see why the easterly and westerly divisions of the Central Provinces have a higher average rate than the two middle divisions, as shown in Map VIII, for in the recent decades cholera has undoubtedly invaded the province from either side, and not simply swept over it from Bengal, as appears to have been the case in former days. The importance of this in supporting the conclusion I have already come to, that Bombay now also has endemic centres of cholera, is evident, and my tables show that cholera is present in nearly every month of the year in the northern Konkan coast area of the Bombay Presidency, including Bombay city, with rapid railway communication with the Deccan and the Central Provinces.

It is very unfortunate that returns are not available for the great Indian-ruled state of Hyderabad, except too limited data for the small cantonments to be of much value, but it will be seen from Map IX that North and South Deccan, the northern central Madras districts and the east central and south-east coast areas of Madras are all connected together by a chain of a high proportion of increased cholera in the same years; much more so than in the single chain down the east coast through the northerly coast divisions from Orissa to Madras. This bears out Cornish's opinion that Madras is rarely infected from Bengal by the direct east coast route, the break usually taking place between the Vizianagram and Godavari districts, with sparsely inhabited hill tracts in the former.

CLIMATE AND THE YEARLY VARIATIONS IN THE INCIDENCE OF CHOLERA.

The yearly variations in cholera incidence and the very important question as to how far they are related to variations in the rainfall, temperature and humidity, remain to be considered as far as time will permit. Diagram II shows the annual cholera rates per mille for the whole of India from 1874 to 1923, only it should be noted that in the years 1874 to 1876 the data are not quite complete, as the Bengal figures then were only for very limited selected areas. It will be apparent at once that the epidemic rises vary much in degree, and appear at most irregular periods, lending no support to the three- or six-year cholera cycle theories, so some other less simple cause must be looked for. As it is clearly impossible in this paper to deal with the epidemics of the whole period, and to avoid any selection of those favouring any particular theory of causation, it will be best to take first the three which caused the highest mortality, namely, those culminating in the years 1877, 1892, and 1900, which are fairly illustrative of the whole period, and include very high incidence in all the major epidemic areas. So if we find any common causative factor in these three, it will be simple to note if that cause was also present in most of the remaining less severe outbreaks.

TABLE I.—YEARLY PROVINCIAL MORTALITIES AND RATES PER MILLE IN 1875-77 EPIDEMIC.

	United Provinces deaths per cent.	Punjab deaths per cent.	Central Provinces deaths per cent.	Bombay deaths per cent.	Madras deaths per cent.
1874 ...	6,464, 0.27 ...	78, 0.005 ...	16, 0.001 ...	37, 0.002 ...	313, 0.01
1875 ...	64,427, 1.33 ...	6,246, 0.36 ...	37,108, 3.66 ...	47,555, 2.94 ...	94,555, 2.82
1876 ...	48,311, 0.85 ...	5,786, 0.33 ...	22,807, 2.38 ...	32,117, 2.63 ...	148,193, 4.07
1877 ...	31,770, 0.74 ...	29, 0.001 ...	3,418, 0.46 ...	57,228, 3.75 ...	357,430, 12.20

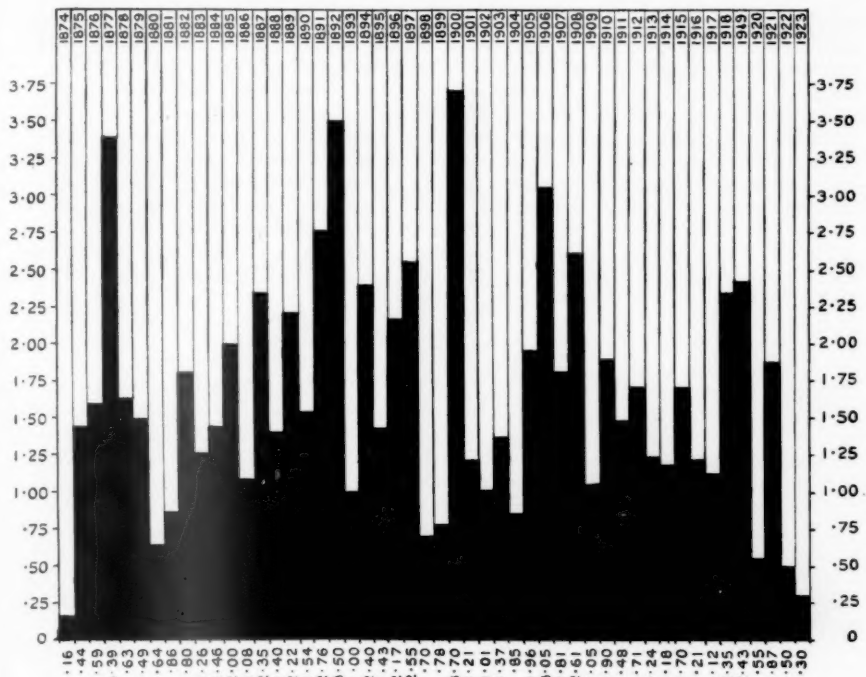


DIAGRAM II.—Annual cholera rates per mille for India, 1874-1923.

THE 1875-77 EPIDEMIC.

This was the most terrible cholera epidemic of Southern India on record, and it followed the lowest known incidence of 1874 with only 30,691 reported deaths, or 0.16 per mille, in all India. It therefore affords a good opportunity of tracing the spread of the disease when railways were far less developed than at present, so I have worked out Map X from the data carefully recorded by S. C. Townsend in the Sanitary Report for India of 1876 and have entered the provincial mortalities from 1874 to 1877 in Table I, from which it will be seen that cholera was much below the average in the endemic areas of Bengal and the United Provinces, and was nearly absent from the Punjab, Central Provinces, Bombay and Madras in 1874. In 1875 it became widespread and epidemic in the Central Provinces, Bombay and Madras, as indicated in Table I by the rates per mille of 50 per cent. and over, in excess of the average rates, being printed in heavier type. It continued to be epidemic in the two southern presidencies of Bombay and Madras in 1876 and 1877.

In map X of the spread of cholera over India during 1875 and 1876, the months in which cholera first became widely prevalent are entered in the United Provinces and the Eastern Punjab of North India, while in the remaining areas 4-75 against the name of a place indicates the month of April, 1875, in which the epidemic was recorded to have first reached that town, and 20-3-75 against Nasik, for example, indicates the date of the first case as March 20, 1875; the arrows show the directions of the spread of the epidemic.

the disease spread in several directions, doubtless once more through returning pilgrims: (1) North to Kandesh, Indore and Rajputana, and up the Nerbudda valley to Betul in the Central Provinces; (2) west through Buldana and Amraoti in Berar to the Nagpur division, which was thus invaded from both east and west; (3) south-west through Aurangabad and Nander to Hyderabad city in the Nizam's dominions; (4) west to Bombay; and (5) lastly, south to Poona in April, and on to the Sholapur and Satara districts in June—with important pilgrim centres materially aiding the distribution of the disease, to Bijapur and Belgaum by July, and to the west coast Ratnigiri and North Kanara districts, in August and September respectively, as shown in Map X.

SPREAD OF CHOLERA IN 1875 IN THE MADRAS PRESIDENCY.

So far this epidemic followed a somewhat similar course to that of 1817, except for the spread north and east from Nasik. But when we turn to the south-east of India we find an even more significant difference between the two outbreaks, for instead of cholera spreading south through the Hyderabad State to invade Madras from the north-west, as in 1817, in the later epidemic the disease, which had been almost absent during 1874 from the Presidency (with the exception of the most northerly Gunjam district adjoining Bengal, with 243 out of the total 313 of that year), had been present extensively in Ceylon at the end of that year and during January to March, 1875. The fact that the first increases this year in April were at Negapatam, the port at the mouth of the Cauvery river in the Tanjore district, and in Tinnevely, the nearest district to Ceylon, indicated the strong probability of its importation from Ceylon, unless it recrudesced from the thirty-three scattered cases of cholera reported in the Tanjore district spread fairly uniformly throughout the whole of 1874. However this may be, there is no possible doubt that cholera spread northwards from Tanjore through nearly the whole of the Madras Presidency during 1875, as shown in Map X, reaching Coimbatore to the north-west and Cuddapah to the north in June; Kistna, east coast delta, in July; Kurnool, in north-central Madras, in August (this was to the south of Hyderabad, which was also invaded from the north in August); the Godaveri delta, north of Kistna, in December; and Vizagapatam, still further north, in February, 1876, completing the spread over India.

If we compare the spread of cholera over India in 1875 with that of the first known epidemic of 1817, we shall be struck by the essential difference between the two. The earlier one spread not only from Bengal and the Eastern United Provinces over all North-West India, but also from north to south over Central India and on through both Bombay and Madras to Ceylon; whereas, in 1875, the disease radiated from Nasik in the Bombay Deccan, which was most likely first infected from the endemic area of the Bombay coast, into the Central Provinces from west to east, where it met the invasion from the United Provinces into the east of the Central Provinces. It also radiated southwards through the Deccan and along the west coast, and south-east through the Hyderabad State; while a third current of the disease invaded Madras from Ceylon, or originated in the endemic centre in Tanjore, and spread north through North-East and North-Central Madras. In short, the disease radiated from the three endemic centres of Western Bengal and Eastern United Provinces; the Bombay Konkan coast through the Deccan and north from Ceylon or South-East Madras, until the whole of India was covered by the epidemic, thus affording most striking confirmation of the conclusions I had arrived at regarding the widespread nature of the present endemic areas of cholera, as illustrated by my Map VIII, which was, as a matter of fact, worked out before I knew any of the details of the 1875 epidemic.

Another great lesson of this outbreak is the important part played by the Allahabad and the Nasik pilgrim centres in originating the streams of cholera which overran the whole of Central and most of Southern India in this fateful year.

The further progress of this epidemic in 1876 and 1877 can be followed by the data in Table I, already referred to, and the Sanitary Commissioner's map of 1876 shows that cholera recrudesced as usual in Bengal and in Madras in January; in the United Provinces from February to May; in the Punjab from June onwards and in the Central Provinces chiefly from March to June; and in the Northern Deccan from May to July. During 1877 the epidemic declined greatly in northern and Central India, and practically disappeared from the Punjab, such epidemics in these areas seldom lasting for more than two years, but in Bombay and Madras, on the contrary, it increased greatly in virulence in 1877 until after the heavy monsoon rains of July to September in Bombay, and of October to December in Madras, which were accompanied by a rapid fall in the cholera rates.

CLIMATIC VARIATIONS DURING THE EPIDEMIC.

The following principal variations from the normal rainfall in the provinces showing epidemic prevalence during this great epidemic afford striking evidence of the importance of the factor of previous prolonged deficiency of the rainfall in predisposing to excessive cholera prevalence. Thus, the high incidence in the Central Provinces in 1875 followed deficient rain in every month of 1874 except July, when there was marked excess, and also low rainfall in four of the first five months of 1875. In Bombay the monsoon was heavy in 1875, although it ceased early in October, but in 1876 the rains were 15 in. below normal and considerably in defect throughout the monsoon months, with the exception of a slight excess in July. The deficiency continued through 1877 to September, with the sole exception of an excess in June, with the result that famine ensued and the cholera-rate for the whole province rose to 3'53 per mille, and for the most famine-stricken South Deccan to 8'14. In Madras a still more disastrous famine occurred, due to a deficiency of 12'12 in. in 1875, and of no less than 32'64 in. in 1876, when there was less than one-third of the normal rainfall. In the two years and ten months from January, 1875, to October, 1877, the rainfall was in material excess only in May, 1877; it almost completely failed in the normal autumn monsoon period of 1876, with 1'45 in. against a normal of 29'62 in., with the result that the cholera-rate rose year by year, as shown in Table I, to culminate in 1877 in the appalling mortality of 12'2 per mille, much the highest for any province of India for the last fifty years of general vital statistics. And, as the Sanitary Commissioner, W. B. Cornish, pointed out the highest rates of 18'0 occurred in the districts with early famine, 11'1 in those with late famine, and only 4'6 per mille in those with no famine. Cornish also recorded the significant fact that the earlier very severe cholera years in Madras in 1833-34, 1853-54, 1865-66, were all periods of very deficient rainfall and drought.

1891-1892 EPIDEMIC.

1890 was a year of comparatively little cholera, the rate per mille for all India having been 1'64, which rose to 2'76 in 1891, and to 3'50 (the highest rate except that of 1900 with 3'70 on record) in 1892. But this terrible epidemic differed from that of 1877 in affecting most severely northern instead of southern India, and so affords an interesting contrast. In 1890, the year of low incidence, the only divisions showing an excess of 50 per cent. over the average yearly rates were the Assam Valley and the north-western Rohilkund and Lucknow divisions of the United Provinces, where a very definite local epidemic occurred quite independently of excess in Bengal, a good example of cholera being endemic in this province. It was especially noteworthy for the fact that it is recorded that the most remarkable feature of the outbreak "was its apparent origin in the hills and 'terai'; also its dissemination to Bijnor with a certain progressive movement from west to east, through Moradabad, Bareilly, Shahjahanpur and Hardoi to Lucknow," that is,

against the prevailing winds—this being quite contrary to Bryden's contention that dissemination against prevailing winds never takes place. Cholera was also carried by pilgrims from Hardwar to at least five districts in the Punjab and spread there.

INCIDENCE AND CLIMATIC FEATURES IN 1891.

Cholera was in excess in all northern India and in Madras in this year, as illustrated by the following records, and by Table II.

Assam.—High incidence in both valleys, spread extensively by pilgrims returning from Bengal.

Bengal.—High incidence in Dacca, Rajshahi and Bihar divisions along the Ganges river. Excess attributed by Sanitary Commissioner to the Ardhodova Jog bathing festival all along the Ganges, which occurs only once in about twenty-seven years, and was very largely attended; many died of cholera on the river in February. It is interesting to note that in the large Purneah district, stretching north of the Ganges in eastern Bihar to the Himalayas, the pilgrims scattered cholera broadcast in the middle of February, but the disease did not become epidemic in the north of the district until six weeks later, at the end of March, that is, when the absolute humidity in this area first rose to over 0'400.

TABLE II.—CHOLERA INCIDENCE AND RAINFALL IN THE 1891-92 AND 1900 EPIDEMICS.

Year	Area	Per mille	Months of deficient rainfall
1891	Bengal	3.26	April-December, 1891, — 14 in.
"	United Provinces	3.60	Late monsoon, very low, June-July.
"	Punjab	0.49	May-September.
"	Madras	3.50	1890, August-December, — 21 in.; and 1891, January-September, — 19 in.
1892	Bengal	3.68	1892, January-October, — 14.8 in.
"	United Provinces	4.15	December, 1891 to June, 1892, except February. Winter absolute humidity very high.
"	Punjab	3.70	November, 1891, to June, 1892.
"	Central Provinces	4.21	October, 1891, to August, 1892.
"	Bombay	2.28	August, 1891, to May, 1892, in Deccan.
"	Madras	2.80	January, May and October-December, 1892.
1900	Bengal	4.86	August, 1899, to July, 1900, except April.
"	Bihar	7.51	September, 1899, to April, 1900.
"	Punjab	1.37	1899, January-December, and 1900, January-August (— 14 in. of 21 in. in 1899).
"	Orissa	6.27	1899, July-December, and 1900, January-July, except October, 1899.
"	Central Provinces	6.64	1899, January-December, and 1900, January-July.
"	Bombay	8.71	1899, May-December, and 1900, January-December, except August.

Rainfall was very deficient in Lower Bengal in 1891 in January, and from April to December, including the monsoon months, and in Bihar from September, 1890, to April, 1891, as well as from July to December last year. It is noteworthy that Orissa in the south-west of Bengal had excess of rain in both 1890 and 1891, and unusually low cholera in 1891.

United Provinces.—High cholera incidence in all the sub-Himalayan divisions except Rohilkund, which had suffered so severely in the previous year. *Rainfall* very deficient from May to November, except in September, 1890, and from March to December, except in September, 1891. The Hardwar Kumb fair in April, with 700,000 pilgrims, in the little affected western division of Rohilkund, passed off without cholera, the hill pilgrims from infected Kamaon being persuaded not to attend.

Punjab.—Moderately infected this year, the two first outbreaks originating among Hardwar pilgrims, where there is a daily influx of 10,000 to 15,000 persons, in addition to the much larger numbers at special festivals. *Rainfall* very deficient from May to December, except in October.

Central Provinces.—Showed excess first in the northern Jubbulpore division, the first cases in many places being returned pilgrims from the United Provinces in March, and was spread further by local Garhakota cattle fair to the Nerbudda division and south to Nagpur. The East Chattisgarh division had a low rate like the neighbouring Orissa division of Bengal. *Rainfall* good in both 1890 and 1891 except in the last quarter of the second year.

Bombay.—Only the Deccan adjacent to the infected western Central Provinces had a high incidence of cholera. *Rainfall* very deficient in the Deccan in 1891 throughout the year, except in July.

Madras.—Cholera epidemic in the central and south-east districts, the rate per mille being higher than in any year since 1877, but slight in the north-east next to the little infected Orissa. The excess was explained by the Sanitary Commissioner as being "in consequence of deficient rainfall in 1891 (18'70 in. below the average of 49'10 in.), many of the tanks and wells which were drinking water supplies, became dry, and people had to use any water they could obtain." The cholera incidence in 1891 can, therefore, be summed up as being due mainly to deficient rainfall and water supplies and to spread by pilgrims.

INCIDENCE OF CHOLERA AND CLIMATE IN 1892.

This year showed the highest recorded incidence of cholera in India as a whole up to then, every province showing excessive rates, but the history is largely a repetition of that of the previous year.

Bengal.—Epidemic rates occurred in the three southern divisions of the Presidency, Burdwan, and especially in Orissa, as well as in western Bihar, that is, precisely those which suffered least in the previous year, a remarkable immunity being noted in the very three districts which suffered terribly in 1891; a good example of the general rule to this effect. There was no especial festival to account for the epidemic this year, but the cause was once more deficient rainfall producing bad water supplies, namely, "drought in October, 1891, failure of the winter rains, and a rainless spring, resulting in an unprecedented scarcity of water." The appalling incidence of 12'09 per mille in Orissa has only been equalled in two other years of the forty-five I have tabulated, namely, in 1889 and 1908, and in both of these there was the same failure of the previous monsoon and succeeding winter rains, leaving no possible doubt as to the aggravating effect of this climatic abnormality. Calcutta also showed very deficient rainfall for the second year in succession, and in severely infected western Bihar the rainfall was extremely deficient from June, 1891, to July, 1892, with the solitary exception of a very slight excess of half an inch in February: all important facts pointing in the same direction.

United Provinces.—These returned nearly 200,000 deaths this year, nearly equalling the record year of 1887, the epidemic of the previous year having continued as a recrudescence after the usual decline in the winter months of low absolute humidity. It is of great interest to note that from October, 1891, to April, 1892, there was a remarkable excess of absolute humidity,—only equalled in the last thirty-four years by the same months in 1893-94, which was also followed by early and excessive cholera in this area. This shows that the recrudescence of the disease was favoured by such unusually high cold weather absolute humidity, as might not unnaturally be expected from the data given in an earlier section of my investigations. The rainfall was again very deficient during the first six months of this year, as well as during the monsoon months of September and October. Nearly every division of the province suffered severely, as illustrated by Map XI, but the Kamaon Hills suffered most, with a death-rate of 11'35 per mille, having been infected by Hardwar pilgrims proceeding to the Garhwal shrine in this hill area.

The Hardwar Pilgrims and the Spread of Cholera.—The most important feature of this year's cholera epidemic in north-western India was the great part played in its spread by the pilgrims visiting Hardwar, the sacred place of exit of the Ganges from the Himalaya mountains, where, in addition to the great bathing festival with 22,000 pilgrims present on March 22, when cholera broke out—and 200,000 more on the way there who were turned back—the other fairs at Hardwar this year numbered sixteen, with from 10,000 to 35,000 present at each. In spite of every sanitary care an outbreak of cholera occurred. This was partly on account of the low rainfall causing the water of the bathing pool to be stagnant. It is recorded that "two sufferers in the last stage of cholera were taken out of the pool and died immediately afterwards," the water not only being drunk as part of the religious ceremony by all the pilgrims, but also taken back with them in bottles and drunk by their relatives and friends very soon after their return home, in accordance with another religious custom, to which outbreaks of cholera in the neighbouring Punjab and Central Provinces have actually been traced. Many pilgrims with cholera were removed from the trains taking them back to their distant homes.

Punjab.—The greatest cholera epidemic since 1867 occurred this year, both epidemics having been spread wholesale over the province by returning Hardwar pilgrims, although it is on record that the spread of the disease was much more rapid in 1891 than in 1867 and 1875, with far fewer railways in the province. The outbreak was favoured by deficiency of rainfall from May, 1891, to June, 1892, leading to scarcity of food and "a general diminution of the supply of water." But the predominant influence of the Hardwar pilgrims is shown by the striking fact that the outbreak at that fair on March 22 was followed by cholera appearing among the pilgrims—rapidly dispersed by rail—in no less than fourteen different Punjab districts between March 24 and March 31 (in all but two instances in returned pilgrims), and in sixteen more districts by the end of April. The Sanitary Commissioner recorded that "the first cases of cholera reported from eighteen of the thirty-one districts in the end of March and the beginning of April occurred in the persons of Hardwar pilgrims, and in many of the villages the disease appeared among the general population very shortly after the first cases among the pilgrims."

Central Provinces.—By far the highest recorded rate of 8·85 per mille occurred in the eastern division in 1892, infection having been brought back by pilgrims returning from the Allahabad fair early in February, who appear to have been infected by passing through cholera districts on their journey, as there was no cholera at that fair this year; this indicates that the danger to pilgrims does not reside solely in cholera actually at the places of pilgrimage. In the Jubbulpore division cholera was again spread by the Garhakota fair, the origin of the epidemic being explained by deficient water supply and drought due to very low rainfall from October, 1891, to August, 1892. Many of the tanks and wells were dried up.



MAP XI.—Cholera incidence in 1892, 3·5 per cent.

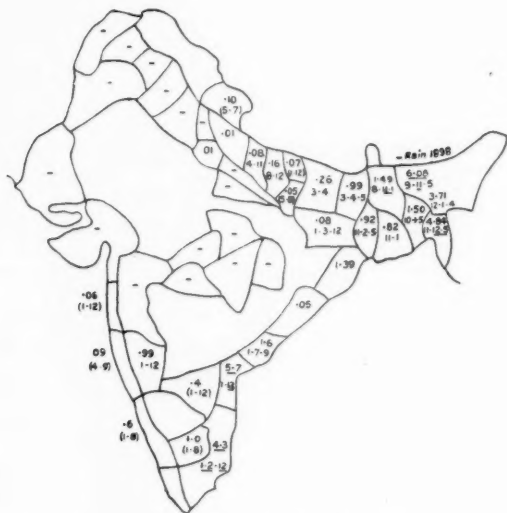
Bombay.—There was a very severe epidemic in the comparatively rarely infected Sind division, due to spread of the disease into its northern districts from the adjacent Punjab.

The whole course of the severe epidemic of cholera of 1892 once more is seen to be influenced mainly by low rainfall, resulting in deficient and impure water-supply, and the spread to be chiefly due to pilgrims infected at the religious fairs, or by passing through infected districts on their return journey.

THE CHOLERA EPIDEMIC OF 1900.

The greatest mortality ever returned in India from cholera since vital statistics of the general population have been recorded was in 1900, with 797,222 deaths, or 3·70 per mille, the distribution of which is shown in Table II. The two previous years showed the lowest cholera rates since 1880 and 1881, the disease having been absent (below 0·01 per mille) in 1898, as shown in Map XII, from all the Punjab, the Central Provinces and the Sind, Gujerat and North Deccan divisions of Bombay. In 1899 it was absent from the three eastern divisions of the Central Provinces, Gujerat and the North Deccan, and was not in excess in a single division. But it is noteworthy that at the end of 1899 cholera increased considerably in Bengal and Assam, and became slightly prevalent in the sub-Himalayan tract of the United Provinces, following a failure of the monsoon with a very early termination of the rains in September, 1899, over all north-west and central India, including Bombay and the Deccan.

The conditions were so uniform over nearly the whole of India in this disastrous year that they may be dealt with more briefly than in the case of the former epidemics.



MAP XII.—Cholera incidence 1898, 0·70 per cent.

Assam showed the very high rate of 6·67 per mille in the Brahmaputra valley, the increase beginning unusually early in September, 1899, and continuing epidemic until the next monsoon began in June, 1900. RAINFALL below normal.

Bengal.—Cholera in excess in the Deccan and Rajshahi divisions from September and October to May. RAINFALL in defect from August, 1899 to July, 1900, except for a slight excess in April, but in September, 1900, a record fall of 45 in. occurred, nearly all in four days, when we were able to boat through the main streets in Calcutta, giving an excess of 25 in. for the year, and leaving a defect of 20 in. in the other eleven months: a good example of the necessity of examining the monthly as well as the total rainfall of any year. The Bihar division of western Bengal showed the record rates of 8·59 and 6·50, and deficient rain from

September, 1899 to April, 1900, except for slight excess in January. Orissa showed the high rate of 7·27, with very deficient rain from July, 1899 to July, 1900, with the exception of excess in October.

United Provinces.—There was excess of cholera in the eastern division, with very deficient rain from September, 1899 to August, 1900, with the exception of a slight excess in January.

Punjab.—The cholera death-rate was the highest on record, with the exception of 1892, over half the total occurring in the famine-stricken districts of the two easterly divisions of Umballa and Jullunder. The rainfall had been in continuous defect from August, 1898, through all 1899, and on to August, 1900.

Central Provinces.—These showed the highest cholera death-rate on record of 6·64 per mille, the eastern division being infected from Orissa and the two western ones from the Bombay North Deccan divisions: RAINFALL very deficient throughout 1899 and up to July, 1900, famine conditions being present.

Bombay also had the record rate of 8·71 per mille, every division showing epidemic prevalence, and the conditions of famine and cholera were described as the most terrible known in the Presidency. RAINFALL at Bombay in 1899 less than half the normal and nearly equally defective in the Deccan, the deficiency continuing until July, 1900, owing to the south-west monsoon being very late.

Madras.—In Central and South-East Madras cholera was also epidemic. RAINFALL very deficient in the north-east monsoon months of November and December, 1899, and throughout 1900, with the exception of slight excess in May; thus completing one long tale of failure of the rains, followed by famine and pestilence.

THE FREQUENCY OF THE RELATIONSHIP BETWEEN DEFICIENT RAINS AND SUBSEQUENT INCREASED CHOLERA PREVALENCE.

Striking as are the foregoing data the years were exceptional ones, and further evidence is required to enable the fact of the frequency of increased cholera after low rainfall to be established. The most convenient way to furnish this at the end of such a lengthy paper will be to tabulate the data of the worst affected areas of the remaining years in which the total cholera mortality in India was considerably above the average, and so are thus unselected except for their high cholera rates. The data are shown in Table III, and the relationship between low rainfall, usually both in the latter part of the previous year, as well as during important periods of the year to which the figures belong, will be seen to have been present, to a greater or less degree, in all the twenty-five examples, with the solitary exception of the United Provinces in 1894. This exception is of great interest as the endemic sub-Himalayan divisions showed high cholera rates in spite of unusually heavy rainfall in both 1893 and 1894, but the cholera death-rate rose from the very low rate of 0·05 per 100,000 in January, to 3·1 in February, and 15·2 in March, thus earlier and more rapidly than in any other year in my extensive tables. It is noteworthy that the absolute humidity remained much above the average from October, 1893, to February, 1894, being at the very exceptional rate of over 0·400 in the latter month, so the recrudescence of the disease in 1894 in this endemic area appears to have been greatly favoured by continued high humidity throughout the cold weather, such as rarely occurs. This factor also appears to come into operation occasionally in other areas, and so is worthy of further consideration than can be given to it in this paper.

Many other examples of increased cholera following deficient rainfall might be given if space permitted, but enough has been said to indicate its importance, although it should be mentioned that high cholera rates by no means always follow low rainfall, as this factor sometimes appears to exercise little effect, especially if a recent serious epidemic has exhausted much of the susceptible material.

TABLE III.—CHOLERA INCIDENCE AND RAINFALL IN EPIDEMIC YEARS.

Year	Area	Per mille	Months of deficient rainfall
1885 ...	Orissa ...	5.27 ...	1884, July-November, and 1885, June-November.
... ..	West Central Provinces ...	4.99 ...	1884, October-November, and 1885, August-November.
1887 ...	West Bihar ...	4.67 ...	1886, + rain; 1887, - rain February and June-September.
„ ...	United Provinces ...	4.54 ...	1886, -10 in. August-September; 1887, rain every month but August.
1889 ...	Orissa ...	12.82 ...	1888, June, July and October; 1889, January-April.
„ ...	Central Provinces ...	5.96 ...	1888, August, September and December; 1889, January-July and September.
1894 ...	United Provinces ...	3.80 ...	1893, + rain; 1894, + rain. Absolute humidity +, November-December and February-March, 1894.
1896 ..	Bengal ...	3.19 ...	1895, January-December, - 22 in.; 1896, January-May and August-December.
„ ...	Central Provinces ...	5.58 ...	1895, September-December; 1896, January-May and September-October.
1897 ...	Orissa ...	6.09 ...	1896, September-December; 1897, May-July and September.
„ ...	Central Provinces ...	6.09 ...	1896, January-May and September-October: 1897, May-July and September.
„ ...	Bombay ...	3.03 ...	1896, September-October; 1897, January-June.
„ ...	Madras ...	4.38 ...	1896, January-July and October; 1897, January-April and October-December.
1906 ...	Bihar ...	4.80 ...	1905, October-November; 1897, April-June and August-December.
„ ...	United Provinces ...	3.14 ...	1905, May-July and September-December; 1897, January and October-December.
„ ...	Punjab ...	3.26 ...	1905, February, August; 1897, January, April-August, October-December.
„ ...	Bombay ...	2.50 ...	1905, March-October and December; 1897, March-June and September-December.
„ ...	Madras ...	3.90 ...	1905, April-September, November-December; 1897, April-May and October-November.
1908 ...	Bengal ...	5.32 ...	1907, April-May, July-November; 1897, February, May and September-December.
„ ...	Punjab ...	0.61 ...	1907, May-July, September-December; 1908, February and September-December.
„ ...	Madras ...	3.90 ...	1907, January-May, July-September; 1908, January, March-August, November-December.
1918 ...	United Provinces ...	2.56 ...	1917, August, October-December; 1918, January-June, August-December.
„ ...	Madras ...	3.00 ...	1917, January-May, September, November; 1918, July-October.
1919 ...	Central Provinces ...	4.46 ...	1918, January-April, July-December; 1919, March-May, September, November.
„ ...	Bombay ...	2.63 ...	1918, June-December, - 47 in.; 1919, February, June, August-December.

PILGRIMS AND THE SPREAD OF CHOLERA.

In addition to the climatic factors by far the most important is the spread of cholera by the millions of pilgrims who yearly travel from one place to another to visit shrines; a vast subject which can only be dealt with adequately in separate studies of each province in relation to its neighbours. But the following facts, in addition to those already mentioned, should be sufficient to convey some slight idea of the influence of the masses of pilgrims who undertake such journeys in each year in India. Every twelfth year especially large gatherings take place at Hardwar late in March or early in April, when one to two millions may collect in a few days, and every one of these gatherings since 1867 has been followed by an epidemic of cholera in the neighbouring Punjab, which in most instances has been more severe than in any of the intermediate eleven years. Similarly, every twelfth year extra large numbers attend the Allahabad pilgrimage about the beginning of February, and every one of these gatherings from 1882 to date has been accompanied by a great rise of cholera in the next few months in the province. But it is very instructive to note that in none of these years was cholera in excess in the Punjab, which is separated from Allahabad by nearly the whole length of the United Provinces, while the fair takes place at a time when the climatic conditions are most unfavourable to the disease in the dry cold

Punjab, including the lowest absolute humidity in India. The Puri pilgrimages are a still more notorious cause of the spread of cholera, in addition to accounting for the Orissa division having the highest average cholera mortality in India; the exceptionally large gathering in 1912 led to the spread of the disease to the neighbouring eastern division of the Central Provinces, as so often occurs from this centre. In the Bombay Province the Pandarpur fair in the Sholapur district of the Deccan has over and over again been responsible for epidemic prevalence not only in the Bombay Presidency, but also in the neighbouring south-western divisions of the Central Provinces. In 1909, a year of exceptionally low cholera incidence in India, a localized epidemic occurred in the Deccan and North Konkan divisions of Bombay and the adjacent Berar division of the Central Provinces, due to a very special festival at Nasik lasting for a year and recurring only at many years' intervals. A similar occurrence in Bengal and Assam in 1891 has already been described. In Madras in 1894 the Sanitary Commissioner, Colonel W. G. King, enumerated ninety-two places of pilgrimage, with a total attendance of nearly 1,500,000 persons, and he and others have recorded the spread of the disease from the Tirupati and other Madras fairs.

Innumerable other instances could be given, but the influence of pilgrimages in India in spreading cholera is so well known, and has been so generally acknowledged since the retirement of J. M. Cunningham (who obstinately refused to admit their effect) that it is unnecessary to labour this factor further, except to emphasize the necessity of taking it into account, in addition to the climatic factors brought out in this paper, when attempting to forecast the epidemic prevalence of cholera in India, and in considering the steps to be taken to limit its spread.

The two greatest factors influencing the monthly and yearly incidence of cholera in India are therefore the following: (1) the variations in the monthly rainfall and absolute humidity in different areas in each year, and (2) the dissemination of the infection by travellers, especially the many hundred thousand pilgrims who yearly undertake long journeys to attend various well-known sacred shrines. The records and data in the voluminous annual sanitary reports of each of the provinces of India require careful study (on which I am now engaged) in the light of facts brought out in the general discussion of the subject in this paper, in order to determine the local conditions influencing the incidence and spread of cholera in relation to contiguous provinces, and to allow of the dangerous zones being recognized each year in time to take steps to minimize the risk of cholera being spread by pilgrims and others visiting the dangerous areas. Fortunately, we now possess in inoculation against cholera a simple and effective method of protecting the pilgrims and other travellers against infection of themselves and, even more important, of bringing back the infection to their households and places of residence. It only requires the additional knowledge, now within sight, as to when such protection should be afforded to them, to enable the attainment of a very material diminution of the spread of cholera over India by pilgrims and others. The epidemic areas, which are sometimes quite free from cholera for a year at a time, could thus protect themselves very largely from invasion by cholera, and in the case of the Punjab this is of international as well as of local importance, for by far the greatest danger of cholera spreading once more in a devastating epidemic from India to Eastern Europe is by the overland route to Afghanistan, as in the great epidemics of 1826-37, 1866-70 and 1892-94, all of which first passed through the Punjab.

CONCLUSIONS.

(1) In the 1817-19 and subsequent cholera epidemics in India, up to those from 1859 to 1871 described by Bryden and Cornish, the disease appears to have spread from its home in Lower Bengal over North-Western, Central and Southern India in a series of waves of two to four years' duration at somewhat irregular intervals, the endemic area, according to Bryden, being limited to Bengal and West Assam.

(2) Since 1877 the monthly cholera mortality for every district in India has been recorded, furnishing far more detailed information than the army and gaol figures of Bryden's time; but they have not hitherto been utilized for a comprehensive study of the incidence and spread of cholera in India, such as is attempted in this paper.

(3) A study of the average monthly cholera incidence and rainfall, temperature and humidity in a diagram and four maps of the seasonal incidence in forty-five divisions of India, shows (a) no uniform relationship with rainfall, as the disease during the south-west monsoon is at its maximum in most parts of India, but at its minimum in Lower Bengal; but it shows (b) a regular great decline or disappearance of the disease in all parts of India when the absolute humidity falls to or below 0'400, such great dryness of the atmosphere preventing the epidemic prevalence of the disease. The months in which cholera first shows a great increase after the winter quiescent period in North-West and Central India are those in which the absolute humidity first rises to over 0'400, the seasonal increase in most parts of India being thus explained quite irrespectively of any spread from Bengal.

(4) The average annual incidence of cholera is highest in Assam, Lower Bengal, Bihar and the eastern sub-Himalayan divisions of the United Provinces of Northern India, and in South-east Madras; all areas with few or no months in absolute humidity below 0'400, and consequent continued prevalence of the disease throughout the year.

(5) The present endemic areas, as shown by the disease never having been absent for a single year in three recent decades, include the areas of high incidence, just mentioned, of Bengal, the United Provinces and Madras, together with the low-lying west coast of Bombay, with the constant absolute humidity of over 0'400, so the endemic areas are now far more extensive and scattered than the parts of Assam and Bengal indicated by Bryden as late as 1869.

(6) The epidemic areas, in which severe outbreaks occur frequently after a year or two of complete absence of the disease, include the south and west of the United Provinces, all the Punjab, the Sind, Gujerat and Deccan divisions of Bombay, and the whole of the Central Provinces. The spread of epidemics in these areas has been studied by means of curves of the annual incidence in forty-five divisions for forty-five years, and in as many yearly maps of the distribution and months of the first annual increase, maximum prevalence and decline for each year.

(7) A map showing the number of epidemic rises in each area, and those in which a rise occurred in the same years in contiguous areas, shows a larger number of epidemics in the United Provinces than in Lower Bengal, so they could not all have originated from Bryden's Bengal endemic area. The studies of the forty-five years maps clearly show that a number of the increases originated in the endemic area of the United Provinces above described, from which they spread over the Punjab with decreasing intensity in proportion to the distance of the divisions from the United Provinces, and the dryness of their climate. Similarly, it is shown that the Central Provinces in recent decades were sometimes invaded from the east, from the southern Orissa divisions of Bengal, occasionally from the north, from the United Provinces, and frequently also from the west from the Deccan divisions, contrary to Bryden's conclusion that cholera always spread from Bengal to the north-west over the United Provinces, or to the south-west over the Central Provinces to Bombay, with the monsoon winds. The facts on which he based his theory are now explained by the effect of low absolute humidity in inhibiting epidemics described in this paper.

(8) The three most severe epidemics of modern times are considered in the light of the foregoing data, and in connexion with the meteorological conditions associated with them. The diffusion of the 1875-77 epidemic is mapped out and shown to have spread, largely through pilgrims, from separate endemic foci, north-west from Bengal and the United Provinces, east and south from Bombay, and north from Ceylon or Southern Madras. In each area of very high incidence the epidemic was

associated with great deficiency of the previous rainfall, accompanied by drought, by bad water supplies, and often by famine. The epidemic of 1891-92 was spread mainly in the first year by a rarely occurring great Ganges pilgrimage, aided by deficient rains, and in the second year by continued deficient rainfall, and especially by the Hardwar pilgrims. The most severe epidemic of all, in 1900, was once more associated with very exceptional failure of both the monsoon and the succeeding winter rains over very large areas of India. A table is also given of the epidemic prevalence in every other of the forty-five years in which the total cholera mortality in India was much over the average. Out of twenty-five affected areas, in no less than twenty-four previous greater or less deficiency of the rains preceded the cholera exacerbations, and in the remaining area in the United Provinces in 1894 very exceptionally high humidity throughout the winter months was followed by a unique early recrudescence of the disease culminating in an epidemic.

(9) By watching the climatic conditions influencing the seasonal and annual incidence of cholera in any area to which attention is now drawn, increased or epidemic prevalence should usually be foreseen in time to enable steps to be taken to lessen its spread by pilgrims and other travellers, by means of inoculating them against the disease before attending religious and other gatherings in cholera-infected districts. The Punjab, Sind, Gujerat and Deccan divisions of Bombay and the Central Provinces, so liable to invasion by epidemics, have largely in their own hands this simple means of lessening their cholera mortality. The sanitation, and especially the provision of a pure water supply, in all important pilgrim centres, should be a first charge on imperial and provincial revenues under reliable sanitary administration.

Discussion.—Sir HAVELOCK CHARLES said that whatever Sir Leonard touched upon he generally contributed something new. He was exceedingly keen upon his work, and, as a rule, he proved himself right. There was no question that there would be much opposition to the points which he brought forward, but that would not detract from the interest which his statements would excite in those who were interested in cholera.

Much could be said about the struggles that had existed in India between those holding different views as to the causation of epidemics of cholera. As important, if not more so, was the prevention of cholera, the question of food and drink, and regarding that little had been said. He hoped that proper notice would be taken of Sir Leonard Rogers' views.

Lieut.-Colonel C. A. GILL, I.M.S., said that it had always been recognized in India that cholera epidemics were in some obscure way correlated with meteorological conditions, but although the air-borne and wind-borne theory had long been discarded, no one had yet succeeded in giving an adequate explanation of the peculiar features presented by cholera epidemics that those shrewd observers, Bryden, Cunningham, and Bellew had relied upon in upholding, almost as an article of faith, the air-borne theory. On the contrary, he (the speaker) was of opinion that modern investigations of cholera epidemics had only served to deepen the obscurity surrounding certain aspects of the epidemiology of the disease. He thought, however, that the thesis put forward that evening by Sir Leonard Rogers, that an absolute humidity equal to an aqueous tension of not less than 0.400 in. of mercury was a controlling factor in cholera epidemics, might well prove to be the means of reconciling many apparently conflicting observations and of explaining much that was at present obscure.

He (Lieut.-Colonel Gill) recalled that the first scientific work upon the relationship of meteorological conditions to an epidemic disease was that carried out by the Plague Commission appointed by the Royal Society, of which Professor C. J. Martin, F.R.S., was President, and the late Mr. Bacot and Dr. St. John Brooks (amongst others) were members. The Commission showed that absolute humidity exercised an important controlling influence upon plague epidemics by reason of its effect on the rat-flea. Similarly, he (the speaker) had shown, in a study of the influence of meteorological conditions on the mechanism of malaria epidemics, that the important part played by humidity was due to its effect on the longevity of the mosquito, and, so far as could be seen, not to any direct effect upon the malaria parasite. In both cases, therefore, atmospheric humidity exercised an influence upon an epidemic disease by means of its effect upon the carrier-insect. Cholera, however, was a disease in which no insect-transmitter was involved and in which it would appear that atmospheric humidity

must exercise a *direct* influence upon the cholera vibrio during its extra-corporeal phase. The validity of this inference could only be determined in the light of laboratory experiments, but, if valid, it would carry implications of profound importance in connexion with the influence of atmospheric states upon the conveyance of other directly transmitted parasites.

Lieut.-Col. J. D. GRAHAM said this was essentially a paper to be studied carefully. He would, therefore, reserve any serious criticism, but take the earliest opportunity on his return to India of bringing it to the notice of all Directors of Public Health and of Research Institutes in India for careful study.

The way in which Sir Leonard had fitted his absolute humidity theory to explain the various epidemics of the past century was both ingenious and remarkable and deserved the closest investigation on the part of all interested. If Sir Leonard were correct in his assumptions, we might be able to explain away much that was at present unintelligible; but we must meanwhile preserve an open mind.

The question of the endemicity of the disease was receiving much attention both nationally and internationally. The eyes of the delegates to the "Office International d'Hygiène Publique" were on India as the cholera plague spot of the world. General Smith could testify to this aspect of the question in Paris, in October, 1925, when a translation of Lieut.-Col. Fry's paper was presented. Lieut.-Col. Gill had told of the way in which the Punjab and Kashmir epidemics of 1925 had pursued their course and had published the details to date. Realizing its importance, the Conference of Research Workers in Calcutta in December last had discussed the subject carefully and, as a result, three inquiries were now in progress, in Bengal under the Director of Public Health, in Asanol mining area (Bengal), and in the Eastern United Provinces under the Director of Public Health, to try amongst other things to elicit the conditions under which, in known endemic villages, the vibrio became pathogenic as we knew it in epidemics. It was hoped that light would, in due course, be shed on the problem. At Singapore, in January last, he had met Dr. Heiser, of the International Health Board of New York, who informed him of the interesting work being done in the Philippines to investigate the conditions under which it was possible for non-agglutinating vibrios to produce clinical cholera. This all showed that there was need for further contributions to knowledge on the subject, and Sir Leonard's paper had, therefore, been read at a very opportune moment.

The question of single or multiple endemic foci was one upon which opinion was sharply divided. If the Director of Health of the United Provinces of Agra and Oudh had heard Sir Leonard's remarks that evening he would probably have expressed his disagreement, as he (the speaker) understood that the Director of Health believed in all his cholera being imported. Perhaps some of the seventeen epidemics in the United Provinces described by Sir Leonard were recrudescences of infection formerly imported from Bengal and therefore not proof of the existence of old endemic foci. Certainly Lieutenant-Colonel Fry's paper, as Major-General Smith could testify, evoked interest and criticism last October in Paris; but if we had three epidemic foci instead of one, the problem increased in gravity, as all the foci would have to be attacked in the near future.

Inoculation as an insurance, as described by Sir Leonard, was the policy of election; but anyone intimately conversant with the native peoples realized how difficult it was in the absence of an epidemic to get the ryot to submit to it. Even the Mecca pilgrims were not yet inoculated under compulsion. Workers in India had, however, developed another side of preventive treatment—that of the oral bilivaccine, and last year, as a result of the work being done in South-East Europe, it was arranged through the League of Nations that two of the Research Department Officers on leave (Lieutenant-Colonel Mackie and Lieutenant-Colonel Gloster) should visit Besredka in Paris and proceed to Warsaw to study at first hand the method of preparation. This they did, and their report was now being circulated. The attitude assumed by the authorities in India was that they must prove or disprove its value before rejecting it. The Director of Health, Madras, was at the moment testing it in the present epidemic in Madras.

He (Colonel Graham) trusted that his remarks would convince Members that India was alive to the unsolved problems connected with cholera and that a solution of some of them might be expected.

Dr. G. CLARK TROTTER asked a question of Sir Leonard Rogers regarding "the eating and drinking of cholera," which had been mentioned by one of the speakers. It had a bearing, he thought, to some extent, on one aspect of this most interesting paper to which they had just

listened; for if the condition and individual resistance of the individual were below par at any time from whatever cause—famine, for instance—or conditions brought about by the weather, then one might expect a greater number to be attacked.

Many years ago, when he was at the Pasteur Institute, an experiment was being carried out with an emulsion of cholera bacilli mixed with soda water. This emulsion had been drunk by the experimenters with impunity, but one of the laboratory assistants, in a fit of bravado, had taken upon himself to do the same, and drank some of the mixture. He fell a victim to a very severe attack of cholera. The theory then advanced was that this attendant, who had been drinking heavily, and had had a bout the night before, was in such a condition that his intestines allowed the vibrio to pass through easily. He would be grateful if the lecturer could state his opinion on the present theories with regard to this aspect, as the question of drinking bazaar milk, &c., had been mentioned in the discussion.

Sir LEONARD ROGERS (in reply) thanked Sir Havelock Charles and the other speakers for their kind remarks about his work. He fully agreed with Sir Havelock's precautions for avoiding cholera in Calcutta and he himself had never allowed uncooked vegetables, such as lettuce, in his house during cholera prevalence. Such factors as alcoholism might predispose to infection by inhibiting the secretion of the hydrochloric acid of the digestive juice, which had great powers of destroying the cholera vibrio and preventing it reaching the small bowel, where it multiplied. The frequency of infection of Mohammedans during the Ramadan fast, when infected water was likely to be taken on an empty stomach, pointed in the same direction. The suggestion that fly infection might be related to the absolute humidity was interesting, as flies had often been suspected to play an important part in carrying the cholera organism to food, &c. The low degrees of absolute humidity which he had found to reduce cholera so greatly might act by drying up the infected evacuation and killing the vibrios before they could reach food or water. When an epidemic occurred among a large assemblage of pilgrims or others it was too late to begin prophylactic inoculation, as all Indian experience showed that the gathering should be broken up and dispersed as rapidly as possible. That was why he advocated the inoculation of pilgrims as far as possible in their own districts before they started on a journey to a pilgrimage in an area likely to be infected at the time. The probable date of this infection could usually be foreseen with the knowledge of the climatic conditions favouring the disease which he had now pointed out. The familiarity of the people with the equally successful plague inoculation would facilitate carrying out his suggestion, whilst, if the important trials of oral cholera vaccine which had been arranged for by Colonel Graham were successful, the use of this oral vaccine would be thereby greatly simplified. During the last few days he had found data in the Punjab Sanitary Report for 1879 showing that no less than 20 per mille of some 45,000 Punjab pilgrims to Hardwar from certain districts died of cholera on the journey or shortly after their return, as well as spreading the disease widely. This mortality could have nearly all been avoided by inoculation beforehand, whilst the priests would be likely to favour its use as they feared cholera might result in closing the fairs.

Section of Epidemiology and State Medicine.

President—Dr. JOHN C. McVAIL.

The Deaths of Merchant Seamen in 1924.

By Fleet-Surgeon W. E. HOME, O.B.E., M.D., R.N.

IN 1924 there were 234,101 men employed on the ships of the merchant marine, of whom 166,913 were British subjects, 12,234 were foreigners, and 54,954 were lascars; their deaths are reported to the Board of Trade if they occur while the men are on ships' articles, or in hospital, discharged from their ships, and the Board, in its annual "Return of Shipping Casualties and Deaths on Vessels registered in the United Kingdom" publishes tables summarizing these reports. It might be thought that an annual medical report on the health conditions of this large body of men, as numerous as the Army, and more numerous than the Navy, would be regularly published, but this is not done. It is therefore important that each of the Board's Returns should be brought before the profession, that the profession may know what is the effect of whatever supervision of health there is at sea, that it may be in a position to decide whether the conditions are satisfactory or whether something more is required. Therefore I was quite glad to be asked by our Secretary for a paper on the subject, as the Return for 1924 had but just appeared.

The tables of deaths in the Return give the deaths reported as having occurred during the year. They are not the total deaths that occurred among men following the industry, but only those men employed on board ships, or in hospital after discharge, that is deaths from tolerably acute illnesses. The death of a man discharged to hospital abroad, recovering there sufficiently to be sent home to England, and dying, not again employed, in England, would not be reported to the Board of Trade and included in the Return. Nor, if a man arrived home in a ship to-day, was paid off to-morrow from his ship in the incubation stage of enteric fever, phthisis, pneumonia or small-pox, from which ultimately he unfortunately died, being taken ill subsequently to his discharge from his ship, would that death appear in the Board's Return. Both these kinds of death, however truly attributable to the men's sea service, would escape the notice of the Board of Trade, and would only be registered with the Registrar-General and fall into the deaths of the general population. In other words the Board of Trade's Return states a great many of the deaths attributable to the industry but not all—probably indeed a much smaller proportion of the attributable deaths than are included in the Annual Health Report of the Royal Navy.

In the Board's Return of the deaths reported, those by injury (homicide and suicide included) are stated in Table VI (reproduced here in Diagram A), those by disease are given in Table VII (here in Diagram B), while Table IX reports the deaths (already included in Tables VI and VII) "regarding which it was stated that drink was a contributory cause"; they have therefore been taken out of the other lists and placed under "alcohol" in Diagram C, in which the facts recorded in Tables VI, VII and IX are combined and re-classified in order to give as complete and correct an account as may be of the deaths reported in 1924, and of their causes.

As we look at these crude figures of deaths we are at once struck by the great

DIAGRAM A.

Deaths on Vessels, 1924.

TABLE VI.—DEATHS BY INJURY.

Cause of death	British subjects	Foreigners	Lascars
1 Foundering	21	1	—
2 Strandings	24	2	—
3 Collisions	15	—	—
4 Missing vessels	59	6	—
5 Fires, &c.	1	2	1
6 Engine room accidents	15	2	—
7 Falls from aloft	8	1	1
8 Falls overboard	54	7	11
9 Washed overboard	12	4	1
10 Falls down hatchways, &c.	26	5	9
11 Killed or drowned (coming on board)	16	—	—
12 Drowned in docks, &c., ashore	71	2	—
13 Killed or missing ashore	4	2	2
14 Drowned bathing	12	—	1
15 Homicide	4	2	2
16 Suicide	28	5	9
17 Missing at sea	42	4	18
18 Other causes	34	7	12
19 Summary	446	52	67

TABLE IX.—DEATHS TO WHICH ALCOHOL WAS CONTRIBUTORY.

8 Falls overboard	1	—	—
10 Falls down hatchways	2	1	—
11 Killed or drowned (coming on board)	5	—	—
12 Drowned in docks, &c., ashore	9	—	—
17 Missing at sea	1	—	—
18 Other causes	4	1	—
Summary	22	2	—

DIAGRAM B.

DEATHS ON VESSELS, 1924.

TABLE VII.—DEATHS CAUSED BY DISEASE.

Group	Nature of disease	British subjects	Foreigners	Lascars
Figures of first crews		166,913	12,234	54,954
A. Specific febrile diseases:				
Enteric fever		29	—	5
Small-pox		8	1	1
Cholera		1	—	—
"DYSENTRY"		7	—	7
Plague		—	—	1
Influenza		4	1	4
Beri-beri		1	3	11
Malaria		28	2	14
Other		13	—	7
B. Constitutional diseases:				
Tuberculosis, lungs		21	8	43
Tuberculosis, other		12	3	15
Cancer		7	1	2
Other		3	—	—
C. Diseases of the nervous system:				
Heat apoplexy and sunstroke		9	—	7
Other		33	5	16
D. Circulatory diseases		55	9	30
E. Diseases of the respiratory system:				
Pneumonia		46	3	49
Other		15	2	13
F. Diseases of the digestive system		37	3	21
G. Diseases of the urinary system		14	2	6
H. Other, ill-defined and unknown diseases		31 ¹	8	21
Total		374	51	273

¹ Includes 4 cases of acute alcoholism.

preponderance of deaths by accidents, which are about half the total instead of the one-twelfth usual among "All Males, England and Wales" of ages similar to those of British merchant seamen (*Lancet*, April 24, 1926, p. 877); the deaths from pneumonia, too, are here only 5 per cent. of all deaths—half the usual proportion; and those from "tubercle (all)" are but 4 per cent. instead of 25 per cent. But it must be remembered that these are deaths of men actually employed on ships, probably all inspected medically when they joined their ships, that is, most likely within three months of their illness, and so with very few chronic cases amongst them. It will also be noticed that the deaths of lascars from pneumonia and tuberculosis are more numerous, absolutely, than those among British seamen, though these last are recorded as three times as numerous.

These figures, then, as they stand, have a certain interest, but they give little valuable information until we can manage to calculate death-rates from them. So we must seek to find figures to represent the average population, daily throughout the year, from amongst which these deaths arose. What the Return tells us is "the number of persons forming the first crews of vessels actually employed," furnishing thereby, as it states, "an approximate basis for estimating the variations in the extent of the risks from period to period," and those numbers for 1924 have already been given. But we are not told for how many months each ship was employed. What proportion of the "first crews" are continuously employed during the year? The Board of Trade, simultaneously with the Census of the Registrar-General, takes a census of seamen in British ships, on that one day, all over the world. That gives us the number of seamen employed, on one particular day at any rate, and that seems a fairer figure to use for our purpose than the figures of "first crews." How do they compare?

	1901	1911	1921
First crews	218,155	234,148	242,440
Census of seamen	186,696	208,214	151,911
Percentage	85	89.7	62

The Census of 1921 was taken in the middle of a great coal strike, so it gives no lead for other years; hence, if we take 90 per cent. of the "first crews," we shall probably get a better approximation to the average number daily employed, and shall not make the death-rate absurdly too low. The figures we are therefore taking for British seamen in 1924 are 150,000, for foreigners 11,000, and for lascars 50,000, and it is with these and similar figures that the death-rates of Diagrams C and D have been calculated. These figures being accepted, we can compare the death-rates of merchant seamen in 1924 with the death-rate in 1921 of "All Males, England and Wales," with the seamen's age distribution (*Lancet*, April 24, 1926, p. 877), when we find that the merchant seamen's rate is about ten times as high for enteric fever and malaria, far higher for small-pox, shows a fivefold liability to death from accidents, and is much higher for alcohol (though there are no quite comparable figures ashore). On the other hand, the seamen employed in 1924 on ships had a death-rate from pneumonia only half the standard, and from tuberculosis still less, about a tenth (we remember that chronic cases are of necessity few among these men), while the total death-rate is, this year, a seventh (14 per cent.) less than the standard, although they had so many deaths from accidents and suffered unduly from some preventable diseases. The figures for two other years, 1901-02 and 1911-12, worked out on the same lines, are compared in Diagram D with those for 1924 for each group of seamen, and at the foot are shown the figures for 1924 expressed as percentages of those comparable in the Return for 1901-02, evidencing the alteration in twenty years. Here it is seen that the only figures to remain constant at 100 are those for pneumonia and tuberculosis among lascars, who continue still to occupy the same (72 c. ft.) statutory space, while the parallel figures for British seamen, who have now two-thirds more space (120 c. ft.) than they had in 1901, have gone down 20 per

DIAGRAM C.
Deaths on Vessels, 1924.

LISTS ADJUSTED.

Cause of death	British subjects	Foreigners	Lascars	Royal Navy 1922 per 1,000	British seamen 1924 per 1,000	Standard rate for seamen
Cholera ...	1	—	—	—	0·01	—
Dysentery ...	7	—	7	—	0·05	—
Enteric fever ...	29	—	5	0·04	0·19	0·02
Influenza ...	4	1	4	0·12	0·03	—
Malaria ...	28	2	14	0·02	0·18	0·02
Plague ...	—	—	1	—	—	—
Pneumonia ...	46	3	49	0·25	0·31	0·58
Small-pox ...	8	1	1	—	0·05	0·0002
Tuberculosis, lung ...	21	8	43	0·37	0·15	1·41
" other ...	12	3	15	—	0·08	0·16
Veneral diseases ...	—	—	—	0·04	—	—
Other infective diseases ...	13	—	7	0·13	0·09	—
Beri-beri ...	1	3	11	—	0·01	—
Cancer ...	7	1	2	0·11	0·05	—
Other general diseases ...	3	—	—	—	0·02	—
Nervous ...	33	5	16	0·17	0·22	—
Circulatory ...	55	9	30	0·11	0·37	—
Respiratory ...	15	2	13	0·13	0·10	—
Digestive ...	37	3	21	0·21	0·25	—
Urinary ...	14	2	6	0·07	0·09	—
Other, ill-defined, and unknown ...	27	8	21	0·11	0·18	—
Total, diseases ...	361	51	266	1·88	2·41	—
Alcoholism, acute ...	4	—	—	0·04	0·03	—
Alcohol, accidents ...	22	2	—	—	0·14	—
Total alcohol ...	26	2	—	0·04	0·17	0·006
Heat-stroke ...	9	—	7	0·02	0·06	—
Homicide ...	4	2	2	—	0·03	0·005
Suicide ...	28	5	9	0·11	0·19	0·14
Casualties to ships ...	132	16	4	—	0·88	—
Accidents on board ...	178	24	48	1·32	1·19	0·47
Accidents ashore ...	82	3	4	—	0·55	—
Total accidents ...	433	50	74	1·45	2·89	—
Total deaths ...	820	103	340	3·44	5·47	6·43

DIAGRAM D.

DEATHS OF MERCHANT SEAMEN, 1901-2, 1911-12, 1924.

DEATH-RATES	1901-2			1910-11			1924		
	British	Foreign	Lascar	British	Foreign	Lascar	British	Foreign	Lascar
Average daily numbers (thousands) 90 per cent. of "first crews" ...	132	31	32	147	25	40	150	11	49
Pneumonia ...	50	—	32	48	—	49	46	—	49
Tubercle (all) ...	45	—	40	39	—	42	33	—	58
Disease ...	555	196	236	466	150	318	361	51	265
Accident ...	978	326	215	742	188	210	433	50	74
Alcohol ...	120	26	4	101	28	1	26	2	—
Total ...	1,653	548	455	1,309	366	529	820	103	340
DEATH-RATES									
Pneumonia ...	0·38	—	1·0	0·33	—	1·2	0·3	—	1·0
Tubercle (all) ...	0·34	—	1·2	0·26	—	1·05	0·2	—	1·2
Disease ...	4·2	6·3	7·4	3·2	6·0	7·9	2·4	4·6	5·4
Accident ...	7·4	10·5	6·7	5·0	7·5	5·2	2·9	4·5	1·5
Alcohol ...	0·9	0·8	0·1	0·7	1·1	0·2	0·17	0·2	—
Total ...	12·5	17·7	14·2	8·9	14·6	13·2	5·47	9·3	6·9

COMPARISON OF DEATH-RATES FOR 1901-2, AT 100 EACH, WITH THOSE
FOR 1924.

	British	Foreign	Lascar
Pneumonia ...	79	—	100
Tubercle ...	65	—	100
Disease ...	57	73	73
Accident ...	39	43	22
Alcohol ...	19	25	—
Total ...	44	52	49

cent. The number of foreign seamen has decreased so much that their parallel figures have not been calculated. It will be observed that rates for both disease and accident have decreased during the period, particularly deaths of lascars from injury, and that the greatest decrease of all is in the numbers of deaths from alcohol among British seamen.

Diagram C shows that the Navy in 1922 had only half the deaths from accidents that the Merchant Service had in 1924; it had less risk from enteric fever and pneumonia, but twice as much from tuberculosis. They cannot, however, be minutely compared, for the Navy is a much younger service and does not drop its sick men so ruthlessly.

With regard to the figures of Diagram C, probably every Member of this Section, in which we regard every disease as something to be prevented, will agree that it is necessary to have some organization: (1) To take care of the inoculation of merchant seamen against enteric fever; (2) to see they get proper prophylactic and curative treatment against malaria; (3) to see they are satisfactorily vaccinated against small-pox before they go abroad (it should not be left to the United States, as in a recent case, to push that on to us); (4) to follow up the history of those who have had pneumonia and tuberculosis in ships without dying from those diseases, so as to secure investigation of the health conditions in the ships in which these cases arose; (5) to make sure that every case of accident is investigated, in order to ascertain that it was inevitably due to the employment, not the result of carelessness or faulty equipment (something like the valuable reports of the Chief Inspector of Factories of the Home Office on Accidents in Docks in his Annual Reports for 1920-21-22, unfortunately since omitted); and (6) to make and publish an annual report on the results of all these activities, and the need for extensions of the work that may be required. We remember, of course, that there has never been a proper medical report on the Merchant Service published anywhere. There is no one formally in charge.

That so considerable an improvement has occurred in the death-rates of the Merchant Marine in the past twenty years may doubtless be set by some to the credit of the Board of Trade. We should certainly have had no knowledge of its extent without the information given by that department, though you will probably agree that very little was due to the initiative of the Board when you have gone a little farther. It is quite a question whether seamen would not have been better off if they had been left entirely to Port Sanitary Authorities under the Public Health Acts, which bring ships in as houses, without the weak powers, want of special knowledge and often conflicting decisions of the Board of Trade. Dr. W. Collingridge, formerly Medical Officer of Health, Port of London, and later Medical Officer of Health, City of London, said in 1897 that the Board of Trade is not a sanitary authority, and has no sanitary officers, its small sanitary powers arising merely from the Merchant Shipping Acts, whereas the Port Sanitary Authorities had ample powers under the Public Health Acts.

There are many indications in support of these deductions made by Dr. Collingridge from his experience. See, for example, in Diagram B, copied pretty closely from Table VII of the Board's Return for 1924, the list of diseases with Beri-beri classed among the specific febrile diseases, contrary to modern practice; note that Tuberculosis is separated from these diseases and classed with Cancer as constitutional, an arrange-

ment thirty or forty years out of date; and see how Pneumonia is still grouped with diseases of the respiratory system, contrary to the more modern classification of the Annual Health Reports of the Army, the Navy and the Air Force. And yet the Board was told two years ago by the Royal Sanitary Institute that this classification was unsatisfactory! As it persists in it, with no medical officer's signature it is not unfair to suppose the Board has at its disposal either no medical advice, or that it gives that advice less weight than it deserves. Considered as a medical report this Return is curious. There is one good thing about it that might be copied with advantage by other departments: it prints in bold type at the head of each page the number of the year, a great help to the student looking up statistics over a series of years. The Return has been signed since the war, not by a medical officer, but—as it primarily contains figures of casualties to ships and only as an afterthought reports casualties to men—by an Assistant Secretary of the Board, a very distinguished civil servant, Mr. A. W. Flux. "Dysentry," the striking misprint in Table VII, in its so conspicuous position, could hardly have escaped the notice of any doctor reading it over, so one doubts whether this table of the Return was ever revised, previous to publication, by a medical man.

How does the Board of Trade come into this, any way? It administers the Merchant Shipping Acts, which deal with the safety of ships, the registration of British ships, wages of sailors, &c., and, incidentally, with a few points of hygiene. The law declares that

"every place in a ship occupied by seamen" shall be "available for the proper accommodation of the men who are to occupy it, and shall be securely constructed, properly lighted and ventilated, properly protected from weather and sea, and as far as practicable properly shut off and protected from effluvia which may be caused by cargo or bilge water."

That is the Board's sanitary charter, all depending on the vague word "properly." The Board cannot compel an owner even to put in a privy for the crew's use, unless he asks for a deduction for tonnage on account of crew space. The Board's surveyors decide, in accordance with their instructions, when the ship is building or being re-surveyed, whether the above conditions are being attained, and much trouble has come to the officers of Port Sanitary Authorities, who have discovered, and tried to remove or better, arrangements that seemed insanitary, but found nothing could be done as the surveyors had accepted things as they were. Anyone who reads the instructions issued by the Board for surveyors, or talks to its officials, will be convinced that the Board is anxious to do the best for seamen, so far as it knows what is wrong and has power to put it right. Yet, under the administration of the Board of Trade, the sanitation of the British Merchant Marine has been an opprobrium. In 1902 Dr. Collingridge said that the sanitary state of ships was fifty years behind that of the rest of the country. Now that condition of ships had been reached under the administration of the Board of Trade. In 1910 Dr. J. Howard-Jones, Medical Officer of Health, Newport, showed that we had lost our pride of place, and were no longer the pattern of sanitation at sea, for in the case of Norwegian ships better sanitary conditions were being insisted upon. Dr. Howard-Jones has pointed out that Norwegian, Swedish and Australian seamen have larger statutory cubic space than the Board of Trade thinks necessary for British seamen.

For numbers of years nothing much was publicly said and recorded about the defects of sanitation on board ships so far as it has been possible to ascertain. But port sanitary authorities were established about the time of the passing of the (1875) Public Health Act, and though at first they were specially concerned with the protection of the country against the introduction of infectious disease from overseas, when this had been controlled they made time to realize their duties towards the seaman (the first article in their instructions), and strove to better his condition. I have been unable to find anything substantial in the way of a complaint before 1894; in that year Dr. Collingridge read a paper on "Practical Points on the Sanitation of Ships," before

the Shipmasters' Society (*Lancet*, May 5, 1894, p. 1111). It was a very wonderful paper to burst forth suddenly out of the silence. Nothing in his long list of needs has proved unrequired, but it was a long time before the Board of Trade accepted some of them, as you will see. His suggested improvements still uneffected are equally needed. You will please clearly understand that all the improvements mentioned in the immediately succeeding paragraphs were asked for by Dr. Collingridge in 1894, over thirty years ago.

In that year, 1894, a new Merchant Shipping Act became law, and in the next year the Board published instructions to its surveyors about crew spaces, which said a crew space *must* have a solid timber deck, a tight drain, and two ventilating pipes, and *should* have bunks, 6 ft. by 2 ft., not less than about 12 in. off the floor, an air-tight casing for the cables if they passed through, a double bulkhead (or partition) to separate it from an adjacent water-closet, and that a water-closet should be ventilated.

After six years the next edition (1900) no longer prescribed 2 ft. as the width of a bunk, and that condition was not again inserted for twenty years.

After twelve years came the Merchant Shipping Act (1906), which ordered for seamen, other than lascars, 120 cubic feet of space instead of 72. It laid down a diet scale for all seamen, and insisted on a certificated cook in all foreign-going ships, also it hinted at the construction of lavatories and bathrooms.

After nineteen years (1913) the new edition, issued, it said, "with due regard to the representations of Sanitary Authorities," perhaps on that account made the greatest advances to be found in any edition. Cable casing *must* be gas tight, there must be no capstan in a crew space or there will be no deduction, heating of one crew space was ordered, and cork cement to all bare iron was ordered, but alas! only in new ships. Also, a table was ordered to be placed in the crew space if no mess room was provided, and there must be a flush for trough closets. A locker for wet oil-skins was advised, separate privies, iron bunks, a hospital, and the paint of the crew space to be white, or light in colour.

After twenty-nine years (1923) crew spaces in new ships were *ordered* to be 6 ft. high below the beams, all crew spaces to be heated (this includes officers' cabins), bunks were again ordered to be not less than 2 ft. wide ("inside measure" being added), "in new ships single seat water-closets, properly partitioned off from one another, are to be provided." And yet "sufficient and suitable" conveniences of such a kind were ordered in all factories more than thirty years before in the Public Health Acts Amendment Act of 1890. Who says we are not discriminated against at sea? The 1923 "Instructions" declared there *should* be baths for the men in ships going abroad, bunks should be metal with metal bottoms, hot fresh water should be available for washing purposes every day.

Other improvements were made during this time, but I am only concerned at the moment with Dr. Collingridge's complaints of 1894, nearly all of which have been remedied. Bunks are still placed against the ship's side, though safety and cleanliness urge otherwise, the daily airing of bedding has not yet come though practised by Captain Cook, the navigator, about 1770, in the "Resolution," in whose cruise of three years only one man died out of a crew of 118 men: a marvellously healthy voyage; and the deckhouse, which appeared during the war, is now again less common, though the *Times* of July 14, 1917, stated that improvement was clear recognition of the consideration seamen had won for themselves during the war.

Why were these improvements delayed so long? Because, I suppose, the Board, having no special knowledge of hygiene, cannot move faster than current shipbuilding opinion, and, as Dr. Collingridge remarked, can be driven back if it is only a matter of hygiene. Its surveyors are good shipbuilders no doubt, and with a sanitary conscience, but not a trained sanitary conscience, like that of a sanitary inspector. A surveyor meets with a condition he realizes to be insanitary, desires to alter it, finds nothing to help him in his instructions, and so leaves the thing alone. Further, it

must not be forgotten that we see crew spaces in all their native uncleanness, whereas the surveyor does not enter them till they are cleansed and cleared, by his instructions; he does not see them at their worst.

In conclusion I would ask, is the Board of Trade, so far as we know, organized to take care of the health of the merchant seamen? Does the Board know that lascars, still with the same statutory space, have now three times as many deaths from pneumonia and tuberculosis as have British seamen, whose space has been increased? If the Board does not know it, why does it not know it? If it does know it, what has it done?

The Board took the advice of sanitary authorities in 1913, and brought out its best-improved book of instructions. It asked the Royal Sanitary Institute in 1924 for advice in classifying disease, and their unchanged Table VII shows what they made of it. What has been the effect on merchant seamen of the Board's want of understanding of sanitary reforms proposed, and want of power to initiate them? It took nineteen years for the Board to order cork cement on exposed iron in crew spaces after Dr. Collingridge had asked for it,—a very simple and inexpensive and very necessary improvement, which we had in the Navy when I first went to sea in 1886, twenty-seven years before the Board nerved itself to order it for new ships. The pity of it is that few see the damaging results of the Board's want of hygienic education, except the medical officers of Port Sanitary Authorities, and what they have thought may be read in *The Journal of the Royal Sanitary Institute*, some excerpts from which have been given in this paper. Dr. J. Howard-Jones's papers in that *Journal* for 1910, in the *Lancet* for 1913 (ii, p. 857), in the *Journal* again for 1915, for 1920, and for 1924 specially deserve to be read. It was the feeling of those officers that led the Institute in 1924 and 1925 to ask that the medical care of seamen should be taken over by the Ministry of Health. The care of the health of merchant seamen is too important for England to be left to any but trained experts, and the medical profession, which rightly takes a stand against all unqualified practice in clinical medicine, when it knows these facts, will hardly support unqualified practice in hygiene for seamen.

Discussion.—Dr. W. M. WILLOUGHBY said that Dr. Home had spent much time and energy in forwarding the interests of seamen. He had raised questions to which a full answer was desirable whatever that answer might be. The tables Dr. Home had constructed removed a small part of the opprobrium which attached to all statistics (though only through the misreading of them). He (Dr. Willoughby) thoroughly agreed with the idea that the medical aspects of the problems which concerned shipping should not be under the non-medical eye exclusively. This was the broad conclusion of the paper.

He (Dr. Willoughby) was more interested in morbidity statistics for seamen than in mortality tables. Dr. Home had fully shown the difficulty of separating the statistics of deaths caused by disease in seamen from those of the populace in general. He (the speaker) did not think they could be separated satisfactorily.

He was not surprised that the Board of Trade tables showed that the sea was deep and difficult to get out of alive, nor was he surprised—he would readily have postulated it from his knowledge of pneumonia, tuberculosis and natives—that the native of India, ill-clad and on a tropical dietary stood a poor chance, as compared with the European, when exposed to the rigors of sea weather, especially in the North Atlantic. He unhesitatingly emphasized (since so much to the contrary had been talked about it) that the provision of 120 cubic feet of space as against 72, in his opinion would not affect the incidence of pneumonia and tuberculosis one jot.

The tuberculous person must not be allowed to go to sea, and every person must protect himself, whether by food or clothing or both, against that depression of vitality by cold which former generations rightly recognized as the prime ætiological factor in the incidence of pneumonia. Let crew spaces be increased by tens of cubic feet, if this could be done without the disservice to the sailor of laying up his ship; nevertheless dilution of germ contact could not be effectively secured, even in good ship's quarters.

Crew space had nothing to do with the twenty-five cases of malaria in a crew of forty-five, on the West Coast, nor with the fact that these cases were amongst Europeans, the whole native crew escaping. In fact, unsalted persons going into a vitality-depressing environment suffered, whether tropic natives voyaging to latitude 45° N., or Britishers proceeding to the tropics.

Pride of place in the world of shipping was a complex matter; if the Port Medical Officer was to share in its upholding he must not lose sight of the fact that his contribution was a part only of that network.

Dr. PHILIP RANDALL congratulated Dr. Home on his success in obtaining definite figures from very unpromising and unreliable information. A medical officer was only borne in a small proportion of the mercantile marine, and the merchant skipper was not, and could not be expected to be, an adept in the reporting of cases of illness occurring on board his ship.

Sir WILLIAM SIMPSON said that the discussion had been mainly directed to criticism on the statistical data brought forward by Fleet-Surgeon Home, but statistics on such a basis, and especially when the majority of the mercantile ships had no doctor, would always be open to controversy. In his opinion, the important point was the unhealthy conditions under which the seamen were housed on board ship. He did not include in this category the large companies such as the P. and O. and the British India, who possessed their own medical officers and an expert medical adviser, but it was the large number of cargo and other ships that carried no doctor. He had travelled in some of them, and he had been much impressed by the fact that, though seafaring was naturally a healthy pursuit, it was greatly neutralized from a health point of view by the low standard of accommodation for the crew and the absence of modern sanitary improvements. He agreed with Fleet-Surgeon Home that the Board of Trade as at present constituted, having no medical department to advise it on matters of hygiene in regard to the housing of the crews of ships, and to see that the regulations were carried out, was not a competent authority in this respect. It had taken thirty years for the majority of Dr. Collingridge's recommendations to be accepted as practicable. This was not a high testimonial in favour of the continuance of the system. The Home Office, which looked after the health interests of the workers in factories and other industries on shore, had its special staff of medical men to inspect these factories and workshops and report on their condition. It was recognized this could only be effectively done by special medical officers. The Board of Trade was apparently of a different opinion.

He strongly supported the views of Fleet-Surgeon Home, and of the Royal Sanitary Institute, that the hygiene of merchant ships and of their crews should be under the control of the Ministry of Health.

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Section of the History of Medicine.

President—Dr. J. D. ROLLESTON.

The Medical Staff of King Edward the Third.

By G. E. GASK, C.M.G., D.S.O., F.R.C.S.

TALES of chivalry, feats of arms and famous victories have flung a glamour of romance over the period when Edward III was Lord of England and half of France. But the underlying tragedy of human suffering has been glossed over, for the old chroniclers, delighting in the narratives of which they were the actors or witnesses, have failed to tell us the fate of those who fell in battle, how they were nursed, or how their wounds were tended. It is only by diligent search of contemporary documents and by inference that we can hope to repair this omission.

Medical histories have little to say about this period, for, with the exception of a brief mention of some surgeons attached to the army of Edward I and the well-known works of John of Gaddesden and John of Arderne, there is a blank until the reign of Henry V. From a perusal of Malgaigne's Introduction to his "*Histoire de la Chirurgie*" one might be led to believe that at that period England had no doctors, or that if they did exist they were of little account. The following notes may help to dispel this impression and prove that Edward III had physicians and surgeons, who though they left no writings behind them, at least served their Sovereign faithfully and deserved the favours he so freely bestowed on them.

These records concern the lives of two physicians and two surgeons who occupied the positions of physician and surgeon respectively to Edward III, and cover a period of over fifty years, roughly from 1317 to 1379. They have been collected from various State documents and are set out in full in an appendix to this paper, which is of the nature of a deductive summary.

It is disappointing for us, but only natural, that the surviving records should deal mainly with gifts of land or money with which the sovereign rewarded his faithful servants, and that details appertaining to the technique of medicine should be omitted. They are, however, of value as indicative of the customs of the times and of the status and mode of life of our medical predecessors.

It appears that it was customary for King Edward III to have attached to his person a physician and a surgeon who accompanied him wherever he went, both in peace and in war; and it is now possible to state their names, the names of some of their relatives and in a few instances the names of the streets in which they lived.

We can also gain a fair idea of the duties expected from these officers, for in the *Liber Niger Domus Edward IV*, or the Black Book of the Household, the commandment and charges for the Doctoure of Physyque and the Maister Surgeon and Potycary are set forth.

The compiler of the exordium or introduction to the Household Book says:

"The house of King Edward 3, was the house of very policy, and flower of England; the first setter of certainty among the domesticks upon a grounded rule; he appointed duties to his offices and officers by a formal and convenient custumal, more certain than was used before his time; he framed his new statutes, commandments, and charges, upon every officer inward and outward; and exercised his acts in honour and profit and honour to himself, and to the favour and great ease of all his liege people."

We may take it, therefore, that the instructions given to the physician and surgeon and apothecary of the household of Edward IV, which are transcribed below, are similar to those which obtained in the reign of Edward III.

Extract from the Liber Niger:—

"Doctoure of physyque," stondith muche in the King's presence at his meles, counceyllyng or awnsering to the King's grace which dyet is best according, and to tell the nature and operation of all the metes. And muche he should talke with the steward, chamberlayn, assewer, and the maister cooke, to devyse by counsaile what metes or drinikes is best accordinge with the Kinge, and when he woll at mete and souper in the King's chambre, devyssing the Kinge's medecines; and dayly havynge in the hall one yoman sitting with the chamberlaynes; takynge dayly for himself to brekefast and souper, in etyng days and lyverey for all nyght, five loves, service from the kyche as squires for the body, one picier wyne, three gallons ale, for all day, if he kepe his chambre: and for winter lyverey, from Allhallowentyde tyll Estyr, one tortayes, one percher wax, two candylls wax, three candylls peris', three tallwood, rushes and litter all the yere of the serjeant usher, and wages and clothing present in the courte as squires of the household; and carriage for one clothe sacke; keeping in this courte two honest servants i all: taking lyverey for his horses in the countrey or towne, by the herberger. This Physycyan, of right and of old custume, should have no part in the generall giftes, gevyn to the houshold, though he were present. Also hym ought to espie if any of this courte be infected with leperiz or pestylence, and to warne the soveraynes of hym, till he be purged clene, to keepe hym oute of courte. There ought no perilous syke-man to lodge in this courte, but to avoyde within three days, and then by favour, as the soveraynes thinke accordinge to contynewe his lyverey, if he logge nygh to the courte, as within a myle, longe or shorte tyme by favoure; and no man to take sycke lyverey at no tyme, but he were an officer. The costes for all medycines belonge to the chamberlayne his audyte in the jewell-house.

"Maistryr Surgeoun" sitting in the King's chaumbre, but most parte in the King's hall, with a person of like servyce, as knyghtes lyverey, takynge at nyght one lofe, one quarte wyne, one gallon ale; and for wynter season one percher wax, two candelles wax, three candells peris', one dim talwod, russes and litter all the yere of the serjeant usher of the hall and chambre; and dayly, if he be present in courte, by the chekker rolle, vii d. and clothing as squyers for the body, or xl s. of houshold; and yerely to hym by petytion allowed in the end of the yere before the Steward, Thesaurere, Countroller, Cofferer, at the countynge-house, for medycynes geven to the sycke and hurt officers, bought by the seyde maister surgeonne xl. s. And if hymselfe be sycke or bleed, then he taketh sycke lyverey with squyers for the body. He hath into this courte lycensed two honest persons, wayters on him, and carryage for his own clothe sacke, by the oversight of the countroller. Also in this office, one yoman surgeon etyng in the King's chambre or hall, if he be one of the numbyr of yomen of the chambre; and for his dayly wages, if he be present in courte, presented in the chekker rolle, iiid. and clothing with the houshold, and chaunces, or xviiiis. He, and the groome of this office, have one honest child or servant into this courte, and lyverey for theyre horses in towne and countrey togyder, by the herberger. To this office is delivered a parte of the old broken mete, clothes and towells, perused in the ewry, delyvered and remembred by the countroller or countynge-house, that may record where they be spent, to make playstys for the sycke officers of this courte, and other longynge thereto. Also this yoman, if he be lette bloode, or othyrwise sycke, he taketh two loves, one messe of grete mete, one gallon ale, for all; and he hathe his competent beddyng, carryed by oversight of countroller for the groomes and hym together; one groome in this office; if he be not admitted groome of chambre, then he sittithe in the halle with groomes of houshold at the towell; he taketh reward and clothing of the countynge house, as othyr lyke of chambre doen; also sycke lyverey. And he setteth for this office, one gallon ale, and in wynter, dim' talwood, two peris' candells, russes and litter for this office, and carryage for his bedd by the countrolloure. And in this office a small coffer, with plaistys and medycens for the King and his houshold, assigned by the countroller. All these persons had byn accustomed to have part, after theyre degrees, of suche giftes as be gevyn generally to the houshold, if any of them be present at the tyme of gevinge; if also they stand not affermed as yoman and groome of the chambre.

"Potycary," etyng in the halle or chambre, amonge, if he be of the numbyr of yomen of chambre, and when, and as often as the ussher of the chambre wolle assigne; takynge wages and clothyng of the countynge-house, lyke to other yomen aforesayde; carryage with one coffyr of the Kinge's stuffe reasonable, by oversight of the countroller and halfe a bedd for hymself and a groome; all the remanent of his medycyns and ingredients, payde of the jewell-house, by oversight of Fysycian, and by audyght of chamberlayn of the Kinge: and if

he be sycke or lett bloode, then he taketh syke lyverey as the yoman surgeon; and parte of the general giftes geven to the houshold, if any be, except alway that suche as be perfectly of the numbyr of the King's chambre, they take theyre part with the chambre and not with bothe; he hath neither groome nor page, but if any able groome be in the ewry.

[*Liber Niger Domus Regis Edw. 4*, published in "*A Collection of Ordinances and Regulations for the Government of the Royal Household*."—*Society of Antiquaries*, 1790.]

It is evident from the above that the duties of these officers were by no means nominal. They had to look after the bodily health of the King and of his officers, and in addition to perform the function of a medical officer of health. It cannot have been an enviable task to supervise the dietary of a monarch, and the fact that they maintained their positions over long periods argues the possession of a large amount of tact.

MASTER PANCIVS DE CONTRONE.

The first physician to the household of King Edward III was one Master Pancivus de Controne or Verona, who occupied a similar position with King Edward II. We hear of him first in the year 1317, when he is described as the King's leech (*Medicus*) and clerk, and was given a grant of 25 pounds a year to be received at the Exchequer at Christmas "as long as he shall remain in the realm."

On account of his name and the fact that he is called in one of the documents Master Pancivus de Verone, it may be guessed that he was an Italian. He had also a brother, named Peregrine de Controne, a merchant, the son of Bonoditus de Controne deceased, who in 1319, 12 Edward II, was granted the custody of the customs of wool, hides and wool-fells in Ireland.

Edward III came to the throne in 1327, and it appears that he took on his father's physician and further rewarded him, for in 1328 it is recorded that he made a grant to Master Pancivus de Controne, King's clerk and physician of the manor of Temple Guyting, co. Gloucester, in place of the 100 pounds granted him previously, and that the grant was made on account of his services to the late king, queen Isabella and the King.

Nothing is known as to the professional status of Master Pancivus, nor where he received his medical training except the inference that he was an Italian. There are references (quoted in full in the appendix) which show that he served King Edward III for some ten years and that a considerable number of grants of land were made to him. There are also records which show that he was a moneyed man and that he had lent money to the Priory of St. John of Jerusalem and also to King Edward himself, for in 1337 the King acknowledges that he received from Master Pancivus the sum of £4,068 16s. 8d, as well as 9 florins royeaux, 5 florins à l'aignel and three florins of Florence.

The last reference that I can find to this physician is an order, dated the 26th May, 1338, to Richard de Foxcote, late Sheriff of Gloucester, to pay to Master Pancivus de Controne, the King's leech, £25 of arrears which were due to his account.

The name of Master Pancivus now disappears from the records, and he presumably died or retired about this date, after twenty years' service to the Royal Household during the reigns of both Edward II and Edward III.

MASTER JORDAN OF CANTERBURY.

The successor of Pancivus to the post of Physician to Edward III was Master Jordan of Canterbury who is described as a clerk in the year 1326, but in a grant given at Antwerp on the 20th November, 1338—the year of our last record of Master Pancivus—he is given the title of "King's physician" and is granted an annuity of 20 marks.

He seems to have been appointed on probation in the first instance, but evidently gave satisfaction for on November 8, 1340, when the King was at Ghent, an order

was issued in which it was stated that the King engaged Master Jordan for life as his doctor, on account of the expert skill he had found in him, and that he was to receive the usual robes and wages at the hands of the keeper of his wardrobe.

Again, in 1343 the King granted him £20 yearly for life, to be received from the men of Dorchester, co. Dorset, in consideration of his great labours and expenses in the King's service on either side of the sea.

Of the many expeditionary forces sent out from this island, aflame with lofty purpose or intent on plunder, there is none which captures the imagination more than that body of men some 40,000 strong which sailed from Southampton in 1347 to spoil and plunder up to the very gates of Paris and to secure undying fame on the field of Crécy. Though small, it was an efficient, highly-organized and well-equipped force with a reputation for shooting which inevitably calls to our minds that other wonderful army which left these shores in August, 1914.

In such a well-equipped force one might have expected the medical service to have been well represented. Unfortunately this was not so. I am unable to find one single reference to medical men in the contemporary accounts of the battle of Crécy, nor mention of any provision for the disposal of the sick and wounded. Military surgeons of ancient times were seldom mentioned and were held in scant esteem. Reluctantly we must come to the conclusion that at this time medical arrangements for the wounded did not exist.

Yet there is evidence that one doctor at least, namely Master Jordan of Canterbury, accompanied the King in his expedition of 1347, shared in the fatigues and anxieties of his march across France and in the astounding triumph of Crécy.

In proof of this contention are the facts that Jordan's name is cited in June, 1346, in the French Roll, as having letters of protection from having to find contributions of armed men, on account of his being about to set out with the King. His name also occurs in Wetewang's *Accounts of the War* (published in vol. xviii of the *William Salt Archæological Soc.*, 1897) where it is stated that he received as wages of war, 109 shillings for a period of three years and a half and 56 days. He was still on active service in the 22nd year of the reign of Edward III, for it is recorded that he again received wages of war, but this time the amount is not given. Of Jordan's subsequent history not much is known, though it is evident that he retained the royal favour; for in 1350 his son William was nominated to receive a pension from the abbot and convent of St. Albans, and in 1352 his two sons Adam and William, in consideration of the good service done by their father, were granted, each of them sixpence a day to be taken yearly by the hands of the sheriffs of London.

In 1352 another notice appears, that, on account of good services done by Master Jordan, the King granted to his daughter, Margaret, the sum of 7½d. a day out of the issues of the City of London, until provision should be made for her by the King, or his heirs, of a marriage or other competent aid. Later in 1359, at the supplication of Master Jordan, the King, by letters patent, granted Margaret the 7½d. a day for life even though she did marry.

Perhaps Jordan felt that this was the last provision he could make for his daughter, for he shortly died, after some thirty-five years of service with the royal household, as the following record proves:—"Master Hugh de Rungeton master of the king's engines is sent to the abbot and convent of St. Augustine Canterbury to have such maintenance in that house as Master Jordan de Cantuar the king's physician (phisicus) in his lifetime had. 1361. June 3."

It seems likely that in his declining years Jordan found asylum in that monastery in which he passed his early life.

RODGER DE HEYTON.

Roger de Heyton was the first surgeon to Edward III, for there is the following entry in the *Calendar of Patent Rolls*, dated March, 1328:—"Grant for life at the request of Edmund, Earl of Kent, to Roger de Heyton, the king's surgeon, of the

custody of the town of Pennanthlu, co. Merioneth, which Madok ap. Adam in his lifetime held by grant from the late king."

The Earl of Kent was the King's paternal uncle and one of the standing council appointed in 1327 to govern for the young King (D.N.B.). He is described by Froissart as "wise, affable and much beloved." What is more likely, then, that Roger served King Edward II as his surgeon even as Master Pancius de Controne was the court physician both to Edward II and Edward III?

That Roger continued in the royal favour is evident from the fact that grants of land were made to him from time to time. In 1331 a property at Aberfrowe was committed to him during the King's pleasure, for which he had to pay a rent as much as others had rendered for it previously. This appears to have been 7 l. a year. But in 1339, in consideration of the fact of Roger staying continually by the King's side, he was released for life of 10 l. of the said rent and later in 1342 there was an order to proclaim a market at Aberfrowe, on every Thursday, and two fairs yearly, to last six days, from which presumably Roger drew fees. Roger, in all probability, did not reside at his Welsh estate; it would have been too far away for him to perform his services and Edward may have found it difficult to provide accommodation, for in 1333 he sent him to the abbot and convent of St. Albans to receive, in consideration of his good service, such maintenance in their house as John le Squiller, deceased, had.

In 1337, however, Roger was well set up, for he received a grant in fee of a tenement in the town of Westminster, which he held till his death.

There seems reason to believe that Roger practised at Westminster in his spare time, because in 1346 there is a record in the Calendar of Close Rolls that Michael (de Ponynges) and Margery (late the wife of Nicholas le Beche) acknowledged that they owed Master Roger de Heyton, surgeon, 20 l. It seems likely that they never liquidated the debt, for in the following year Michael was killed and Margery ravished.

The question as to whether Roger was present at the battle of Crécy must, I am afraid, remain undecided. It seems clear that he was intended to partake in the expedition, for in the French Roll, dated May 15, 1346 (vol. xviii, *William Salt Archaeological Soc.*), is preserved a writ to the Bailiff of St. Albans: "to exonerate the King's beloved Magister, Roger de Heyton, the King's surgeon, who was about to set out in the King's service, from any contribution to find armed men on account of his lands and tenements in that town." According to the Chronicler, Thomas Walsingham, he held property in St. Albans near the Fish Shambles (*Gesta Abbatum Monasterii Sancti Albanis*, Rolls Series, Vol. ii, p. 358). Unfortunately Wetewang in his "Accounts of the War" does not mention Roger's name and so whether he sailed with the expedition or not must remain in doubt. Perhaps his health failed him, for he died on May 13, 1349.

We know the exact date of his death owing to the fact that there was some dispute as to the ownership of the house in Westminster, and an Inquisition was taken at Westminster, Monday after St. John the Baptist, 28 Edward III, to inquire as to the lands and heirs of the said Roger. The finding was that the messuage was held of the King in chief by service of 2 d. yearly. It was worth 20 s. yearly before the staples (stapule) were set up (errecte) and now 40 s. yearly.

He left a widow named Isabel, and two daughters, Alice and Isabel, both under age.

MASTER ADAM ROUS.

For the next ten years after the death of Roger de Heyton I cannot find any record of a surgeon, and it is not till the year 1359 that we meet the following entry in the Calendar of Close Rolls:—

"Master Adam Rous, the king's surgeon, is sent to the abbot and convent of Croyland, to receive such maintenance in that house for life as Henry atte Nayse, deceased, had therein at the king's request."

6 Gask : *The Medical Staff of King Edward the Third*

The next entry is in 1361, when the King granted to Rous the lease for life of a messuage and four shops in the Poultry in the City of London, a messuage in Lombard Street, and three shops in Berchernerislane.

In 1372 this property was further granted to him "in fee," that is to say, he was given the freehold, and later we find Rous disposing of them in his will.

In 1372 we find that Rous is profiting again by a grant from the King of certain property in Essex.

This is the last reference to be found in which Master Adam Rous is described as the King's surgeon. His royal master Edward III died in 1377 and it seems unlikely that he remained in the service of his successor, Richard II, for, in an indenture, dated May 25, 1379, made with Robert de Swyllington he is described as : "Master Adam Rous of the Poultry surgeon in the city of London."

In that year Rous died, for his will was proved and enrolled in the Court of Husting on Monday the Feast of St. James, Apostle, July 25, 1379.

In his will he desired to be buried in the monastery of St. Albans, and he left numerous bequests, among which was one to the new work of St. Paul's and the reversions of certain tenements to the Prior and Convent of S. Bartholomew de Westmythfeld. He left his wife, Juliana, a certain tenement in the parish of All Hallows for life, and to William Bowyer, his son, he left property in the parish of S. Andrew upon Cornhull and house property to his brother William. To Sir William Stodeleye he bequeathed a girdle with pouch and knife, given him by the Duke of Lancaster.

There is no evidence to show where Adam Rous came from, where he was educated or what was the quality of his work. His very name may be only an indication of the colour of his hair and not his surname as we mean it now. From the fact that he was a citizen of the City of London and that he left property in his will to the Prior of St. Bartholomew's and that one William le Rous was at one time Master of St. Bartholomew's Hospital, it is tempting to believe that Master Adam Rous was once a brother of that Hospital and gained there that knowledge of surgery which secured him later the proud position of the King's surgeon. Unfortunately, though, for that theory William le Rous, the master of the hospital, died in 1338 (Norman Moore, "History of St. Bartholomew's Hospital"), and could not have been Adam's brother William mentioned in the will. The place of the early training of Adam Rous must remain a matter for conjecture only.

These extracts, extending over a period of fifty years and covering the reign of Edward III, bear evidence as to the lives of two physicians and two surgeons who, as far as I know, have not previously been mentioned in medical histories.

Unfortunately none of them has left any medical writings or personal records, so that we can only guess at the methods they employed or where they received their medical training.

Were they lay brothers who picked up scraps of medical lore in their monasteries or had they attended the medical schools of Oxford, Paris, Montpellier or Bologna ? There is no evidence to tell. It is a pity they left no writings, but there is no reason on that account to believe that they were inferior in practice to famous men such as Henri de Mondeville, or John of Arderne, who by their works prove that medicine of the fourteenth century attained a very high standard.

Arderne must have been familiar with all the men we have been mentioning and it is pleasant to think that he may have been their colleague in many of the campaigns in which they participated.

"All these are quiet now, or only heard
Like mellow'd murmurings of the distant sea."

APPENDIX.

EXTRACTS FROM THE LIVES OF

MASTER PANCIUS DE CONTRONE, King's physician. Floruit 1817-1838.

MASTER JORDAN OF CANTERBURY, King's physician. Floruit 1326-1360.

MASTER ROGER DE HEYTON, King's surgeon. 1328. Died 1349.

MASTER ADAM ROUS, King's surgeon. 1359. Died 1379.

MASTER PANCIUS DE CONTRONE.

Calendar of Patent Rolls. 11 Edward II. 1317. November 11. Windsor.

"Grant to Master Pancius or Panecius, the king's leech (Medicus) and clerk, of 25 l. a year to be received at the Exchequer at Christmas so long as he shall remain in the realm."

Calendar of Patent Rolls. 12 Edward II. 1318. August 14. Nottingham.

"Grant to Master Pancius de Verone, king's clerk and leech, of 25 l. a year to be received at the Exchequer so long as he remains within the realm."

Calendar of Fine Rolls. 15 Edward II. 1322. July 2. York.

"Grant for life to the King's clerk and doctor, Pancius de Controne, in allowance of the 100 l. yearly which the king granted to him at the Exchequer so long as he should stay in the realm, and for good service, of the manor of Chiselberg, co. Somerset, and the manor of Brembelteigh and Lavertye, co. Sussex, late of Francis de Aldham, the king's enemy and rebel of late, and the manor of Plescis, co. Hertford, late of Bartholomew of Badelesmere, the king's enemy and rebel of late . . ."

(This grant confirmed by Edward III, see Calendar of Patent Rolls. 1 Edward III. 1327. February 28. Westminster.)

Calendar of Letter-Books of the City of London. Edited by R. R. Sharpe. Letter Book E. Introduction, p. xiii.

Sir Bartholomew de Badlesmere.

In 1321 in the reign of Edward II his Queen, Isabella was on her way to Canterbury, and sought the hospitality of Leeds Castle, co. Kent, the mansion of Sir Bartholomew de Badlesmere, but found the gates closed against her by Lady Badlesmere in the absence of her husband. This insult provoked Edward to take up arms. The City of London sent him a contingent of four hundred men, and with their aid he succeeded in capturing the castle. October 31.

Calendar of Patent Rolls. 16 Edward II. 1322. December 10. Haddlesey.

"Master Pancius de Controne, staying in England, has letters nominating John de Balscote his attorney in Ireland for one year."

Calendar of Patent Rolls. 16 Edward II. 1322. April. Westminster.

"Master Pancius de Controne, staying in England, has letters nominating John Marsuppini of Florence his attorney in Ireland for two years."

Calendar of Patent Rolls. 16 Edward II. 1323. April 19. Westminster.

"Acceptance at the instance of Master Pancius de Controne, king's clerk and of the household, of the collation by R. bishop of Winchester of Nicholas de Figino for his security to the church of Havont."

Calendar of Patent Rolls. 19 Edward II. 1325. August 28. Langdon.

Here

"protection is given to Master Pancius de Cantrone going with the king beyond seas on his service."

Calendar of Patent Rolls. 19 Edward II. 1325. December 12. Tower of London.

"Pardon at the request of Master Pancius de Controne, king's clerk and doctor, to Castruccijs alias Construccijs de Anterminellis for the death of Ciacus Roncinus; and of the abjuration of the realm which he made on that account, as is said."

Calendar of Patent Rolls. 19 Edward II. 1325. December 27. Bury St. Edmunds.

"Pardon, at the request of Master Pancius de Controne, the king's doctor to Leuin de Luca for the death of John Cacheger."

Calendar of Patent Rolls. 19 Edward II. 1326. June 3. Saltwood.

"Peregrine de Controno, merchant, going beyond seas, has letters nominating Pancius de Controno and Ascelinus Simonet(ti) as his attorneys in England for one year."

Calendar of Patent Rolls. 1 Edward III. 1327. March 10. Westminster.

"Grant to Master Pancius de Controne, the king's clerk and physician, of a yearly sum of 100 l. out of the farm of the town of Northampton, until he be provided with land of that value for life."

Calendar of Patent Rolls. 1 Edward III. 1327. December 2. Nottingham.

"Acceptance, at the instance of Master Pancius de Controne, king's clerk and one of his household (familiaris), of the gift and provision by the pope of the church of Havont, in the diocese of Winchester, to Byndus de Byndynelles; and grant thereof to him for life."

Calendar of Patent Rolls. 2 Edward III. 1328. March 1. York.

"Grant for life to Master Pancius de Controne, king's clerk and physician, of the manor of Temple Guytyng, co. Gloucester, in the king's hands by reason of the rebellion of Hugh le Despenser the younger, in place of the 100 l. granted to him on the 10th March last out of the farm of the town of Northampton until he be provided with land of that value, for life, and which latter grant was made to him in compensation for lands granted to him by the late king and subsequently taken from him, at the suit of certain men, by the last parliament of Westminster."

(N.B.—He was granted a 100 l. yearly at the Exchequer on surrender of the manor of Guytyng. May 11. 1328.)

Calendar of Patent Rolls. 2 Edward III. 1328. September 25. Teford.

"Grant for life to Master Pancius de Controne of the manor of Gutyng and other hamlets to the value of 40 l. a year, in part satisfaction of the grant to him of 100 l. a year for his services to the late king, queen Isabella and the king; the remaining 60 l. he is to receive at the Exchequer until he be provided with land of that value."

Calendar of Patent Rolls. 3 Edward III. 1329. May 20. Canterbury.

"Protection with clause 'volumus' for Master Pancius de Controne, the king's physician, going beyond the seas with the king. Master Pancius de Controne, king's physician also going, has letters nominating (as his attorneys understood) Thomas de Sibethorp and Jakettus de Luk' until the feast of St. Peter at Vincula."

Calendar of Patent Rolls. 3 Edward III. 1329. September 27. Gloucester.

"Grant for life to Master Pancius de Controne, the King's physician, of 100 l. at the Exchequer until he be provided for life with land or rent of that value, for his services to the King, the late King and Queen Isabella, and for his better maintenance."

Calendar of Patent Rolls. 3 Edward III. 1329. September 23. Gloucester.

"Grant to Master Pancius de Controne, the King's physician, in fee simple, because he has been anew retained for life, of the manor of Guytyng, co. Gloucester . . . (as before 2 Edward III)."

"(Vacated because otherwise in the roll of the fourth year under the same date.)"

Calendar of Close Rolls. 4 Edward III. July 23. Woodstock.

"To Simon de Bereford, escheator this side Trent. Order to take into the king's hands the 4s. of yearly rent in Foxcote specified below, and to deliver it to Master Pancius de Controne, the king's clerk and physician, together with the issues thereof from 23 September last, upon which day the King granted to him the manor of Guytyng, together with all lands and rents that belonged to Hugh le Despenser the younger"

(Hugh le Despenser was executed as a traitor in 1326 and his head fixed on London Bridge.—D.N.B.)

Calendar of Close Rolls. 4 Edward III. 1330. September 14. Nottingham.

[Extract.] Here is an order confirming the one above and with it a statement to the effect that the King intended Master Pancius to be provided with 100 l. of land yearly for life.

Calendar of Close Rolls. 4 Edward III. 1330. April 3. Woodstock.

"Brother Thomas Larcher, prior of the Hospital of St. John of Jerusalem in England, acknowledges that he owes to Master Pancius de Controno 1250 marks: to be levied, in default of payment, of his lands and chattels and ecclesiastical goods in co. Northampton.

Calendar of Close Rolls. 4 Edward III. September 12.

[Extract.] Brother Larcher seems to have died, for Brother Leonard de Tibertis makes a similar attestation a few months later.

Calendar of Close Rolls. 5 Edward III. 1331. August 6. Clipston.

. . . "Order to deliver to Master Pancius de Controne, the king's physician, 62s. of yearly rent in the town of Weston Brut, whereof Hugh le Despenser the younger was seised . . ."

Calendar of Close Rolls. 5 Edward III. 1331. March 5.

"Memorandum that Master Pancius de Controne came into chancery at Suthwerk and acknowledged . . . " [extract] satisfaction of all debts due to him and also to his late brother Peregrine de Controne, from the Prior of the Hospital of St. John of Jerusalem.

(This sum seems to have amounted to 4,896 l. 16s. 8d.).

Calendar of Close Rolls. 5 Edward III. July 18.

"Richard de Peshale knight, acknowledges that he owes Master Pancius de Controne 10 l. 9s. 0d., to be levied in default of payment, of his lands and chattels in co. Sussex."

Calendar of Close Rolls. 6 Edward III. 1332. April 10.

"Brother Leonard de Tibertis, Prior of the Hospital of St. John of Jerusalem in England, acknowledges for himself and his successors that he owes to Master Pancius de Controno 8,000 marks"

Calendar of Patent Rolls. 6 Edward III. 1332. March 27. Tower of London.

[Extract.] "Commission to make inquisition in the presence of Master Pancius de Controne, king's clerk, concerning 62s. of rents in Weston Brut, co. Gloucester. It is recited that the king had lately given to Pancius the manor of Gutyng, co. Gloucester, and the commissioners are to enquire who was seized of the rent on the day of the forfeiture of Hugh le Despenser and whether the same is a parcel of the manor of Weston Brut or Gutyng."

(There seems to have been a considerable amount of difference of opinion on this point.)

Calendar of Patent Rolls. 7 Edward III. 1333. June 4. Tweedmouth.

"Grant to Master Pancius de Controne, the King's leech, of 100 l. yearly of the ferm of the city of Norwich, in lieu of the like sum granted to him at the exchequer."

(Vacated at surrender and otherwise below.)

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Calendar of Patent Rolls. 8 Edward III. 1334. November 10. Newcastle-upon-Tyne.

"Protection and safe conduct until the Purification, for Master Pancius de Controne, king's clerk and leech, and his men, coming to the king in Scotland with some things of his."

Calendar of Close Rolls. 7 Edward III. 1333. June 4. Tweedmouth.

"To the treasurer and barons of the exchequer. Order to cause due allowance to be made to the bailiffs of Norwich in the ferm of their town for the sums they have paid to Master Pancius de Controne, the king's leech, by his order, as the king lately granted to the said Pancius for his good service to the late king, and to himself, and to retain him in his service, 100 l. for life, to be received yearly at the exchequer, until the king should provide him with 100 l. a yere of land or rent for life"

(Vacated because it was surrendered and is otherwise below.)

Calendar of Close Rolls. 8 Edward III. 1334. December 1. Roxburgh.

"Order to deliver to Master Pancius de Controne, the king's leech, a rent of 62s. in the town of Weston Brut, together with arrears . . ."

Calendar of Close Rolls. 10 Edward III. 1336. June 3.

[Extract] Pancius de Controne made a gift of a tenement in the parish of St. Mary Magdalen, Southwerk to Henry de Hattone.

Calendar of Patent Rolls. 8 Edward III. 1334. December 10. Roxburgh.

"Writ de intendendo directed to the tenants of the manor of Gutying, the hamlets of Kynton, Berton, Thornhull, Holford and Cotesdon, the towns of Beryngton, Little Risyngdon, Sloughtre, Frompton Felde, Gloucester (and twenty-four other hamlets and towns set forth) in respect of their homages, fealties, rents and other services due to Master Pancius de Controne, king's clerk, by virtue of the grant made to him on 23 September, 3 Edward III, of the manor as an escheat of Hugh le Despenser the younger with everything which the latter held in right of the same on the day on which he forfeited his lands to Edward II."

Calendar of Patent Rolls. 9 Edward III. 1335. April 18. Clipstone.

"Grant to queen Philippa of the custody, during minority of the heir, of the lands, late of John de Seinteler, tenant in chief, with the issues from the day of death of the said John and the marriage of the heir.

Mandate in pursuance to the following—

William de Northo,
Robert Selyman,
Ralph de Middelneye,
William Erneys—

Master Pancius de Controne, who was appointed to the custody of some of the lands, as is said."

Calendar of Patent Rolls. 9 Edward III. 1335. June 7. York.

"Grant to Master Pancius de Controne, king's clerk and physician, of 50 l. yearly for life, payable at the exchequer, or from the first custody, marriage or lands falling into the king's hands which he is willing to receive as the equivalent."

Calendar of Patent Rolls. 9 Edward III. 1335. October 18. Roxburgh.

"License for Master Pancius de Controne, the king's physician, to grant in fee or for term of years as he will to any of the king's allegiance but not in mortmain, the manor of Gutying, held in chief, with its hamlets and members, knights fees, advowsons of churches, and all other appurtenances as fully as he holds it by grant of the king."

Calendar of Patent Rolls. 11 Edward III. 1337. August 30. Westminster.

"Acknowledgement of the king's indebtedness to his physician, Master Pancius de Controne in 4,068 l. 16s. 8d., received from him in the treasury, and in 46 l. 13s. and nine florins ryals, five florins of the lamb, and three florins of Florence, a loan; with promise to repay these."

Calendar of Close Rolls. 11 Edward III. 1337. July 28.

"Order to deliver to Master Pancius de Controne, the king's leech, or his attorney, all the lands, possessions, benefices, goods, chattels of the men of the power of the king of France in co. Gloucester and not to intermeddle therewith."

Calendar of Close Rolls. 11 Edward III. 1337. October 17. Westminster.

"To the treasurer and barons of the exchequer and to the chamberlains. Order to deliver to Master Pancius de Controne, the king's leech, the sums in which the king is bound to him, or to give a competent assignment therefor, when he may quickly be satisfied, receiving from him the king's letters obligatory, as the king is bound to him in 4,068 l. 16s. 8d. which the king received from him in the treasury, and in 46 l. 13s. and nine florins royeux, five florins à l'aiguel, and three florins of Florence, lent by him to the king."

Calendar of Close Rolls. 12 Edward III. 1338. May 26. The Tower.

"To Richard de Foxcote, late sheriff of Gloucester. Order to pay to Master Pancius de Controne, the king's leech, 25 l. of the arrears of his account, as the king granted to Pancius 50 l. yearly, and ordered the treasurer and chamberlains to pay him 25 l. for Easter term last, and they have certified that they have not the money with them at present."

Papal Letters—in Vol. 2 of the Calendar of Papal Registers, p. 532.

1336. 17, Kal. Oct., Pont de Sorgue (f. 260 d.).

"To the archbishop of Dublin. Mandate at the request of the king and queen Philippa, to grant a dispensation to John son of the late Peregrinus de Controno, of his diocese, of illegitimate birth, to be ordained and hold a benefice.

Ibid. To the bishop of London. The like in favour of Master Pantius de Controno, physician."

JORDAN DE CANTUARIA.

Calendar of Patent Rolls. 20 Edward II. 1326. July 22. Westminster.

Protection with clause nolumus for Master Jordan de Cantuaria, clerk.

Calendar of Patent Rolls. 12 Edward III. 1338. November 20. Antwerp.

"Grant to Master Jordan de Cantuaria the king's physician, of an annuity of 20 marks at the exchequer, until he receive an equivalent of land or rent."

(Vacated by surrender, and he has other letters patent of 20 l. from the form of the town of Dorchester, enrolled in August, 17 Edward III.)

Calendar of Patent Rolls. 14 Edward III. 1340. November 8. Ghent.

"Engagement for life, on account of the expert skill which the king has found in him, of Master Jordan de Cantuaria as his doctor, with the usual robes and wages to be received yearly at the hands of the keeper of his wardrobe, whether he be present in the King's house or absent from it."

Calendar of Close Rolls. 15 Edward III. 1341. October 4.

"To William de Cusuancia, keeper of the Wardrobe. Order to deliver to Master Jordan de Cantuar(ia) the accustomed robes and wages of the King's leech, from 8 November last, on which day the King retained him as his leech, on account of his skill, granting him the customary robes and wages to be received yearly in the wardrobe for life, whether he is present in the King's house or not."

Calendar of Close Rolls. 17 Edward III, Vol. 7, p. 174. 1343. August 18.

"To the bailiffs of Dorchester for the present or the future. Order to pay to Master Jordan de Cantuar(ia), the King's physician, or to his attorney, 20 l. yearly for life of the ferm of that town, as the King granted that he should receive 20 marks yearly at the exchequer, and he surrendered the letter patent to Chancery to be cancelled, and in consideration of his great labours and expenses in the King's service on either side of the sea, the King granted him the 20 l. yearly which the men of Dorchester, Co. Dorset, render yearly for the ferm of that town, to be received of the hands of the bailiffs for life."

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Calendar of Patent Rolls. 18 Edward III. 1345. January 18. Westminster.

Grant to Master Jordan de Cantuaria, the king's physician, for his service in staying continually with the king, of the eight marks which the bailiffs of Melecombe, co. Dorset, pay yearly for the farm of their town until the king provide him with an equivalent of land or rent in England for life.

(Vacated and surrendered, and the eight marks are granted to Peter de Brugge by letters Patent on the patent Roll of the twenty-sixth year under date of September 3.)

Calendar of Patent Rolls. 20 Edward III. 1346. March 25. Westminster.

Pardon to Roger, son and heir of Roger de Wilmyngton, who held of Reginald son of Herbert, late under age and in the king's ward, by knight service, for marrying Margaret, daughter of Thomas de Horton, brother of the king's clerk, Master Jordan de Cantuaria, the king's physician, without license.

Calendar of Patent Rolls. 1345. April 12. Westminster.

"Jordan de Cantuaria, the King's physician, is sent to the Prior and Convent of Christchurch, to receive such maintenance in that house as Master John de Stratford, deceased, had there at the King's request, in consideration of his services on either side of the sea, the King on the said 18 Aug: granted to him for life, by other letter patent these 20l. which the men of Dorchester, Dorset, render yearly for the ferm of that town."

Calendar of Patent Rolls. 20 Edward III. 1346. March 25. Westminster.

Grant to Master Jordan de Cantuaria, king's clerk, the king's physician, of the keeping of two parts of the lands late of Roger de Wilmyngton, who held by knight service of Reginald FitzHerbert, late under age and in the king's ward, which are extended at 12s. 10d. yearly, to hold with all things pertaining to the custody during the nonage of Roger, son and heir of the said Roger.

Calendar of Close Rolls. 21 Edward III. 1347. November 3. Westminster.

To the Treasurer and Barons of the exchequer. Order to allow eight marks yearly to the bailiffs of Melcombe, co. Dorset, in the ferm of that town, if they find that they paid eight marks yearly to Master Jordan de Cantuar(ia), the king's physician, as the king granted to him eight marks to be received yearly of that ferm for life, and ordered the bailiffs to pay him the said eight marks yearly.

Calendar of Close Rolls. 23 Edward III. 1350. November 18.

William, son of Master Jordan de Cantuar, the King's physician, is nominated to receive a pension from the abbot and convent of St. Albans by reason of the new creation of the abbot.

Calendar of Close Rolls. 24 Edward III. 1350. November 18. Westminster.

"To the bailiffs of Dorchester for the present or the future. Order to be anserable to Master Jordan de Cantuar(ia), the King's leech, for what is in arrears to him for twenty marks yearly from 18 Aug: in the seventeenth year of the reign and henceforth, as the King granted him 20l. to be received yearly at the Exchequer, which letter Jordan surrendered to Chancery to be cancelled."

Calendar of Patent Rolls. 26 Edward III. 1352. September 3. Westminster.

[Extract] License for the king's clerk, Master Jordan de Cantuaria, the king's physician, to grant to the king's serjeant, Peter de Brugge, the 25l. 6s. 8d. of rent out of the town of Dorchestre and Melecombe, co. Dorset, granted to him for life by letter patent of the king

Calendar of Patent Rolls. 26 Edward III. 1352. October 22.

"Granted for life or until they be promoted by the king, in consideration of good service done by the king's clerk, Master Jordan de Cantuaria, the king's physician, to Adam de Cantuaria and William, his brother, sons of the said Jordan, to wit to each of them 6d. a day, to be taken yearly by the hands of the sheriffs of London; or if for reasonable cause they cannot at any time be satisfied by these, by the hand of the treasurer and chamberlain of the king."

Calendar of Patent Rolls. 27 Edward III. 1353. October 25. Westminster.

"Grant for good service done by the King's clerk, Master Jordan de Cantuaria, the king's physician, to Margaret, daughter of the said Jordan, of 7½d. a day out of the issues of the City of London until provision be made for her by the king or his heirs of a marriage or other competent aid."

(Vacated because surrendered, and she has other letters patent under the date of September 16, in the thirty-third year, whereby the King granted that, although she has married, she shall have the said 7½d. a day.)

Calendar of Patent Rolls. 33 Edward III. 1359. September 16. Leeds Castle.

"Whereas the king by letters patent granted to Margaret daughter of Master Jordan de Cantuaria, king's clerk, his physician, 7½d. a day out of the issues of the city of London until he provided for her in a marriage or other competent aid; at the supplication of the said Jordan and on surrender by Margeret of the letters patent, he has granted that she shall take the same, even though she marry, for life or until provision be made for her in an equivalent of land or rent."

Calendar of Close Rolls. 35 Edward III. 1361. June 3.

"Master Hugh de Rungeton master of the king's engines is sent to the abbot and convent of St. Augustine Canterbury to have such maintenance in that house as Master Jordan de Cantuar the king's physician (phiscus) in his lifetime had."

ROGER DE HEYTON.

Calendar of Patent Rolls. 2 Edward III. 1328. March. York.

"Grant for life at the request of Edmund, Earl of Kent, to Roger de Heyton, the king's surgeon, of the custody of the town of Pennanthlu, co. Merioneth, which Madok ap. Adam in his lifetime held by grant from the late king."

Calendar of Fine Rolls. Edward III. Vol. 4, 1331. January 12. Westminster.

Commitment during pleasure to the king's yeoman, Master Roger de Heyton, the king's surgeon, of the rhingildship of the cantred of Aberfrowe, with the demesne of Aberfrowe, at the yearly rent at the exchequer of Kaernarvon of as much as others have rendered for the same hitherto.

Calendar of Close Rolls. Edward III. 1333. January 19. York.

"To the abbot and convent of St. Albans. Whereas the king lately sent his surgeon, Master Roger de Heyton to them, in consideration of his good service, to receive such maintenance in their house as John le Squiller deceased, had therein by the late king's order, and they have done nothing concerning the order, as Roger has informed the king: the king therefor repeats the former order, any other order to the contrary notwithstanding. If there be any reason why they should not obey it, they are to certify the king thereof."

Calendar of Fine Rolls. 1335. February 2. Roxburgh.

"Grant for life to the king's servant, Master Roger de Heyton, the king's surgeon, for good service, of the rhingildship of the cantred of Aberfreu in North Wales with the king's demesne lands and the portership there, at the yearly rent at the exchequer of Kaernarvon of as much as Yereward Voyl of Vyllour deceased rendered."

Calendar of Fine Rolls. 1336. December 20.

Appears an order that Roger de Heyton shall render 7l. yearly for the above grant.

Calendar of Patent Rolls. 2 Edward III. 1337. December 1. Guildford.

Granted in fee to Master Roger de Heiton, the king's surgeon, of a messuage or tenement in the town of Westminster, an escheat by the death without heir of John Dacres who held it in chief.

Be it remembered that the heirs of the said Roger sold the messuage to the king for 20 l. and surrendered these letters and so they are cancelled.

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Calendar of Patent Rolls. 13 Edward III. 1339. July 9. Kennington.

"Whereas the king lately granted to Master Roger de Heyton, his surgeon, the manor of Aberfrowe in North Wales, to hold for life for a rent of 39l. 12 $\frac{1}{2}$ d. at the exchequer of Kaernarvan, in consideration of his services in staying continually by his side he has released to him for life 10l. of the said rent."

Calendar of Close Rolls. 15 Edward III. Vol. 6, p. 308. 1341. November 15. Stamford.

"To Robert de Hamburi, chamberlain of North Wales. Order to permit Roger de Heyton, the King's Surgeon to hold the Manor of Abrefrowa in North Wales quit of the rent of 29l. 12 $\frac{1}{2}$ d. thereon, as the King granted him that manor to hold for life, rendering the said rent yearly at the Exchequer of Karnarvon, and on 8th October last, at the request of William de Bohun, Earl of Northampton, the King pardoned Roger the said ferm in recompense for the wages, robes and medicines which he received of the King at the Wardrobe."

Calendar of Close Rolls. November 15. 1341.

To the Treasurer and Barons of the Exchequer. Order to discharge both Roger and the Chamberlain of the said rent from 8 October last.

Calendar of Close Rolls. 16 Edward III. Vol. 6, p. 633. 1342. June 8. Hadleigh.

To the Justice of North Wales or to him who supplies his place. Order to proclaim a market at the Manor of Abrefrowe in that land, which Master Roger de Heyton, the King's Surgeon, holds for life, on every Thursday, and two fairs yearly to last six days, to wit, one on the feast of St. Edward the Confessor and the two following days, and the other at Corpus Christi and the two following days, in accordance with the King's grant to Roger.

Calendar of Close Rolls. 20 Edward III. Vol. 8, p. 66. 1346. May 9.

Michael (de Ponynge) and Margery (late the wife of Nicholas la Beche) acknowledge that they owe to Master Roger de Heyton, surgeon, 20l. to be levied as aforesaid.

(Cancelled on payment.)

Calendar of Patent Rolls. 23 Edward III. 1349. June 19. Westminster.

Grant for life to the king's yeoman Reginald de Rudlond of a messuage by the gate of the Palace of Westminster, which Master Roger de Heyton, late the king's surgeon, had in his life time.

Calendar of Inquisitions. Edward III. Vol. 10. 146. Roger de Heiton or Heyton.

Writ to enquire as to the lands and heir of the said Roger, 3 March, 1354, 28 Edward III.

Westminster. Inq. taken at Westminster, Monday after St. John the Baptist, 28 Edward III.

Westminster. A messuage held of the king in chief by service of 2d. yearly. It was worth 20s. yearly before the staples (stapule) were set up (errecte) and now 40s. yearly.

He held no other tenements in the county.

He died on 13 may, 23 Edward III from which time until now Reynold de Rodlond has been in possession of the said messuage by gift of the king to him for life. Alice, aged 19 years and more, and Isabel, aged 18 years and more, daughters of the said Roger are his heirs. C. Edward III. File 126 (2).

Calendar of Charter Rolls. 1354. January.

[Extract] Roger's house at Westminster was given with others by Edward III to the Dean and Canons of the Chapel of St. Mary and St. Stephen. Perhaps this was why there was an enquiry.

Calendar of Close Rolls. 28 Edward III. 1354. July 18. Westminster.

John de Thorp and Hugh le Peyntour of St. Albans acknowledge that they owe to Roger de Chestrefield, clerk, forty marks: to be levied, in default of payment, of their lands and chattels in the county of Hertford.

Enrolment of indenture witnessing that whereas John de Thorp and Hugh le Peyntour of St. Albans are bound to Roger de Chestrefield, clerk, in forty marks by the precedeing recognisance, Roger grants that if Alice and Isabel, daughters and heirs of Master Roger de Heyton, some time the king's surgeon, who are now under age, half a year after they are of full age, levy a fine or are ready to levy a fine in the king's court for the king's use and at his cost, for a messuage with appurtenances in Westminster, which messuage at one time belonged to Roger, or if their heirs do the like in case they die before they have levied such fine, the recognisance shall be null. Dated Westminster, July 20, 28 Edward.

Calendar of Patent Rolls. Edward III. 1354. § December 1. Westminster.

"Pardon to William de Northbrok of Stepelmorden of his outlawry in the county of Hertford for non-appearance before the justices of the Bench to answer Isabel late the wife of Roger de Heyton touching a plea that he render an account of the time when he was her receiver; he having now surrendered to the Flete prison, as Roger Hillary, chief justice has certified."

Calendar of Close Rolls. 46 Edward III. 1372. April 28.

[Extract.] It appears here that—

the heirs of Roger de Heyton, the king's surgeon deceased, made a release and quit claim to the king and his heirs for the tenements in the town of Westminster.

ADAM ROUS.

Calendar of Close Rolls. 33 Edward III. 1359. March 24.

Master Adam Rous, the king's surgeon, is sent to the abbot and convent of Croyland, to receive such maintenance in that house for life as Henry atte Nayse, deceased, had therein at the king's request.

Calendar of Close Rolls, June 18, 50 Edward III, shows that Rous had certain tenements in the Poultry granted to him for life.

Calendar of Patent Rolls. 35 Edward III. 1361. 4 November. Westminster.

"Grant for life to the king's surgeon Master Adam le Rous of a messuage and four shops in the parish of St. Mildred in la Poetrie, a messuage in the parish of St. Edmund the King in Lumbardestrete, and three shops in Berchernerislane, in the City of London, which are extended at 8 marks yearly beyond reprises and charges incumbent on them, and escheated to the King because Alice, daughter of Peter le Rous of Grenestrede who held them of him in chief died without heir, as has been found by inquisition taken by John Pecche, mayor of the city and escheator there."

Calendar of Patent Rolls. 46 Edward III. 1372. September 1. Wallingford.

"Grant in fee to Master Adam le Rous, the king's surgeon, of the messuage and shops in London granted to him for life by letters patent dated 4 November, 35 Edward III."

Calendar of Patent Rolls. 48 Edward III. 1374. February 26. Westminster.

"Grant to Master Adam le Rous, the king's surgeon, in recompense of two grants of 10 l. yearly at the Exchequer by letters patent, surrendered, dated 16 May in the thirty first year, and 1 October in the thirty second year respectively, of the 20 l. yearly which the executors and assigns of Thomas de Lodelowe, deceased, and the barons of the Exchequer, are held to pay yearly for the keeping of two parts of the manor of Westillebury and Plomberg, co. Essex, late of Thomas Vaghan, 'chivaler,' who held in chief, during the nonage of his heir; grant also that, if the heir gain full age during the lifetime of Adam, he shall have the 20 l. yearly at the Exchequer again, as granted in the said letters patent."

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Calendar of Wills proved and enrolled in the Court of Husting, London. Edited by R. Sharpe. Part 2, p. 275.

A.D. 1379.

Monday the Feast of S. James, Apostle (25 July).

Rous (Adam), surgeon.—To be buried in the place appointed by him in the monastery of S. Alban. Bequests to the new work of S. Paul's, to the Abbey of S. Alban for a pittance the church of S. Alphege within Crepulgate, and divers orders of the friars in London. To Sir William Stodeleye he leaves a girdle with pouch and knife, which the Duke of Lancaster gave him. Directions as to burning of tapers at his funeral and their subsequent disposal. To Juliana his wife he leaves a certain tenement in the parish of All Hallows called "le Mechele" for life; remainder to the Abbey of S. Alban on condition that his obit be observed as directed. Also to his said wife shops in la Roperye near a tenement called "le hood on the hoop" in the aforesaid parish for life; remainder to the Abbess and Convent of the Minoreesses of S. Clare without Aldgate; also the reversion for life of a tenement upon Cornhill after the decease of William his brother and of Johanna wife of the same; remainder to house of the Salutation of the Mother of God of the Carthusian Order near London. To William Bowyer his son and to Lora, wife of the same, a certain tenement in the parish of S. Andrew upon Cornhill in tail; remainder to the aforesaid house of the Salutation. To the Prior and Convent of the church of S. Bartholomew de Westsmythfeld and reversions of certain tenements and rents in the parishes of S. Andrew de Holbourn, S. Edmund the King in Lumbardestrete, and All Hallows the Great in the Ropery. Pecuniary bequests to the wife and children of Simon his brother, to Friar Thomas, son of his brother William, Cristina Harpsfeld, to his servants and others.

Dated London, 27 April, A.D. 1379.

Reference. Calendar of Wills. London Court of Husting. Edited by R. Sharpe. Part 2, p. 61.

The will of Michael de Northburgh, bishop of London who wrote an account of the campaign of Edward 3.

He left the sum of two thousand pounds for the foundation of a house according to the ritual of the Carthusian Order in a place commonly called "Neuchirchewawe" where ther is a church of the Annunciation of the B. V. Mary, which place and patronage he acquired from Sir Walter Manny.

(The following footnote explains.)

"When the Black Death was raging in 1349 he purchased a parcel of land lying in a place called "Spittle Cross," from its belonging to S. Bartholomew's Hospital, afterwards called "New Church Haw," and caused the same to be consecrated for a burial ground. In 1371 he also caused a house of Carthusian monks to be built there, and to be called the "Salutation." (Stow's Survey, Thom's ed., p. 161.) (See will of Adam le Rous.)

Calendar of Close Rolls. 2 Richard II. May 25, 1379. Westminster.

"Indenture made between Sir Rohert de Swyllington the uncle and Master Adam Rous of the Poultry surgeon in the city of London, witnessing a grant with warranty to the said Adam and his heirs of seven messuages, four tofts, eleven bovates of land, 4d. of rent and a rent of 1 lb. cumin in Normanton and Sutton upon Sore co. Notyngnam, rendering 100s. a year, and after Adam's decease 10 l. a year, power being reserved to distrain for arrears of the first mentioned rent, and to enter and hold premises if the rent of 10 l. be in arrear. Dated the manor of Savoye near the city of London. 20 May. 2 Richard 2. French."

Section of the History of Medicine.

President—Dr. J. D. ROLLESTON.

Voltaire and Medicine.

By J. D. ROLLESTON, M.D.

PART I.

IN an address on Voltaire in his relation to natural science, delivered nearly sixty years ago before the Royal Prussian Academy of Sciences, the celebrated Berlin physiologist Professor Emil du Bois-Reymond remarked that the true reason for the neglect of Voltaire in the first half of the nineteenth century, after the high reputation which he had enjoyed in the eighteenth, was that, paradoxical as it might seem, we were all in a sense Voltairians without knowing it.

"The ideals of tolerance, mental freedom, human dignity and justice for which Voltaire had struggled with indefatigable zeal, passionate devotion and every intellectual weapon including his terrible mockery, had become,"

the professor continued,

"a natural element of life like the air we breathe, which we only notice when we are deprived of it. In short, what had once appeared an audacious thought when it had flowed from Voltaire's pen had now become a commonplace."

It is gratifying, however, to find that within recent years, as the result of more profound research, there has been a revival of interest in Voltaire, as has been exemplified in the domain of *belles lettres* by the studies of Lanson, Bellesort and Ascoli, while his pioneer work in anthropology has formed the subject of an interesting communication by Dr. Georges Hervé,¹ a former president of the Société française de l'Histoire de la Médecine. But with the exception of the paper by the late Pierce Bailey on "Voltaire's Relation to Medicine," and the Paris thesis by Boissier entitled "La Mort de Voltaire," little attention has been paid of late to the medical aspect of Voltaire's life and works.

I propose, this afternoon, to deal with Voltaire's relations with individual doctors and the medical profession as a whole, including some account of his own medical history, and to discuss at the following meeting his other relations with medicine.

Voltaire's attention to medical matters, though partly a manifestation of his interest in every department of human activity, was doubtless mainly due to his own feeble health. He frequently describes himself in his correspondence as "l'éternel malade." It will therefore not be out of place to consider briefly the chief points in his medical history.

Voltaire was the last of five children, and is said to have been born in the seventh month, but in any case was at birth (November 21, 1694) a puny infant, who was not expected to survive. He contracted a severe attack of small-pox at the age of 29 (*Correspondance*, Lettre à Mme. la Présidente de Bernières, July, 1723, and October, 1724; Lettre à M. le Baron de Breteuil, December, 1723), but apart from influenza

¹ *Revue de l'École d'Anthropologie de Paris*, 1908, xviii, p. 225.

in 1743 (*ibid.*, Lettre à M. le Comte d'Argental, March, 1743), erysipelas in 1753 (*ibid.*, Lettre à Marquis d'Argens, February 16, 1753), and pneumonia in 1762 (Lettre à d'Argental, April 27, 1762), he does not appear to have had any other acute infectious disease.

He seems to have been subject to chronic dyspepsia from an early age (*Correspondance*, Lettre à Thieriot, 1721; M. le Comte d'Argental, October, 1755), and to have had frequent attacks of colic (*ibid.*, Lettres à l'Abbé Aumillon, October, 1742, Mme. de Fontaine, August 7, 1750, Comte d'Argental, April 27, 1751), particularly during his residence at Potsdam (1750-1753), where he lost nearly all his teeth (Lettre à Mme. de Fontaine, June 17, 1752, Lettre à M. Bagieu, December 19, 1752), and suffered from scurvy (Lettre à Darget, 1751). As early as 1736 he told Cideville that he was dying of a disease of the bowels (Lettre à M. de Cideville, February 22, 1736).

His letters show that he frequently suffered from catarrhal bronchitis, sometimes associated with deafness and aphonia (Lettres à d'Argental, April 27, 1762; Cardinal du Bernis, May 15, 1752; Mme. du Deffand, July 1, 1764). He often complained of febrile attacks which may have been malarial in origin (Lettres à Thieriot, June 30, 1731; Cideville, December, 1731; Mme. du Deffand, April 3, 1769; Marquis de Florian, April 5, 1769), and on at least two occasions (Lettre à Thieriot, August 24, 1724; unpublished English letter to Thieriot in "Voltaire, Montesquieu and Rousseau in England," by J. Churton Collins, p. 277) declared that he had a "double tertian" or "a violent ague."

At the age of 67 (Lettre à d'Argental, February 16, 1761), and again at 77 (Lettre à Mme. du Deffand, March 16, 1771), he alludes to his attacks of gout.

He says that he had an apoplectic attack in 1767 (Lettre à Frédéric II, January 5; Lettre à Damilaville, January 7, 1767); and others in 1775 (Lettres à d'Argental, November 6, Lekain, November 14, 1775), and in 1777 (Lettre à M. le Marquis de Richelieu, March 28; Frédéric, April; Marquis de Villette, May 17, 1777). These attacks, whatever they were, cannot have been at all severe, for we find no interruption in his correspondence at any of these dates.

During his residence in the neighbourhood of Geneva, at Les Délices, Tournay and Ferney, he frequently complained of "ophthalmia" whenever there was snow on the ground. Writing to Cardinal de Bernis (January 6, 1764) he says, "I have become a little Tiresias or a little Tobit." From a letter to d'Argental (Feb. 1 1764) we learn that Tronchin treated him in one of ten attacks with a soothing ointment containing corrosive sublimate, but on another occasion he assured Mme. du Deffand that his eyes were almost cured by a *remède de bonne femme* (April 22, 1765). His eyesight, however, as a rule remained remarkably good throughout life, and his secretary, Wagnière, declares that he never wore spectacles.¹ We shall probably not be far wrong in accepting Rattel's retrospective diagnosis of ciliary blepharitis as an explanation of Voltaire's eye troubles.

Some years before death he began to suffer from symptoms of enlarged prostate. In letters to d'Alembert (February 12, 1773), and d'Argental (February 12, 1773), at the age of 79 he complained of violent attacks of strangury, of which he had a recurrence the following year (Lettre à d'Argental, March 21, 1774).

Boissier has convincingly shown that Voltaire's death was due to uræmia following cystitis secondary to prostatic hypertrophy. The autopsy showed enlargement of the prostate, chronic cystitis, acute nephritis, and an absence of any pulmonary disease to account for the hæmoptysis which occurred some weeks before death and was probably connected with hypertension.

There does not appear to be any foundation for the legend of his terminal coprophagia, and the combined action of uræmia and opium tended to render his

¹ *Mémoires sur Voltaire*, 1826, i, p. 94.

death-bed peaceful apart from occasional outbreaks of delirium, on which Tronchin dwells with a self-righteous and unprofessional complacency.

There is no evidence that Voltaire suffered from venereal disease, in this respect being very unlike Casanova, whose numerous attacks I have discussed in a previous paper before this Section.¹ It is true that the question has been raised by Roger whether Voltaire had syphilis, because Bellosse's pills, of which mercury was an ingredient, were ordered for his eye condition. In a letter to d'Argental (June 29, 1761) he exclaims: "What have Bellosse's pills to do with the eyes? What relation has a pill to the lacrymal gland?" It is probable, however, that the pills were prescribed merely for their purgative effect without an idea of a syphilitic taint being present.

Although he always keenly resented the imputation that he was in good health or that he was not so ill as he pretended to be, it is difficult to avoid the conclusion, in reading his correspondence, that Voltaire always tended to exaggerate his ailments, especially to escape the attacks of his enemies. Indeed, on more than one occasion he admits as much, as when he says to d'Alembert, "Non omnibus aegroto" (May 19, 1754), and to Mme. du Deffand, "Illness is not without great advantages. It frees one from society" (November 1, 1773). Hypochondriasis undoubtedly accounted for a number of Voltaire's ailments. According to his own account he enjoyed the best health when he was busy with his new house and grounds at Ferney. In a letter to Mme. du Deffand, dated April 25, 1760, he writes:—

"I have never been less dead than I am at present. I have not a moment free. Oxen, fields, buildings, and the garden occupy my time in the morning, all the afternoon is devoted to study, and after supper we rehearse plays."

Throughout his life Voltaire insisted on the importance of a regimen and sobriety, especially in food, and there is no doubt that his attainment of such an advanced age in the full possession of his faculties was due to his practising, with occasional lapses, what he preached. The importance which he attached to a regular evacuation of the bowels is illustrated in several passages in his correspondence. During his residence in England he told Thieriot that he had found a special instrument for the administration of enemata (May 27, 1727), and in a letter to Mme. du Deffand (March 3, 1754) he says that one of the gifts that he would require in a wife would be the ability to administer enemata rapidly and pleasantly.

During his long and eventful life Voltaire was brought into contact with medical men on numerous occasions, both professionally and socially. Moreover, his writings, particularly the *Correspondance*, the *Dictionnaire Philosophique*, the *Contes*, and to a less degree the historical works and miscellaneous essays and pamphlets abound in references to the medical profession. It is a remarkable fact, however, which does not appear to have been noted by any previous writer, that, in striking contrast with those of Molière, in none of his plays, particularly his comedies, does a doctor figure as one of the *dramatis personæ*, nor are there more than one or two vague references to medical matters in any of them (see *Charlot*, Act II, Scene 7; *Les deux tonneaux*, Act III, Scene 1). This is all the more surprising, as in the stories, especially *Candide* (Chap. II, XXII, XXIV, XXVIII); *L'Homme aux quarante écus* (Chap. V, XI); *L'Ingenu* (Chap. XIX); *L'Histoire de Jenni* (Chap. V); *Così Sancta* and *Les Oreilles du Comte de Chesterfield* (*passim*), medical men play a more or less prominent part.

The explanation of doctors not figuring in any of his plays may perhaps be found in the following passage in the *Vie de Molière*. Speaking of *L'Amour Médecin*, the first play in which Molière held doctors up to ridicule, Voltaire says:—

"They were very different from the practitioners of to-day. They almost always went about in a gown and bands and spoke in Latin. Even if the doctors of to-day do not under-

¹ *Janus*, 1917, xxii, pp. 115-130.

stand nature better, they have a better knowledge of the world and know that the great art of the doctor is to please. Molière may have helped to abolish their pedantry, but the customs of the time which have undergone a complete change have helped still more."

The change in the outward appearance of medical practitioners since Molière's time is also alluded to in Voltaire's comments on Pascal's *Pensées*. Pascal had said that if medical men had not had gowns and slippers, and doctors had not had square caps and gowns four times too large for them, they would never have imposed upon society, which could not resist this display. Voltaire remarks that a doctor would incur ridicule nowadays if he came to feel the patient's pulse and examine the stools clad in a gown (*Dernières remarques sur les Pensées de Pascal*, XCIX).

About half a dozen medical men who attended Voltaire professionally are mentioned in the *Correspondance*. The earliest of these was Gervasi, who treated him for small-pox, in 1723, by bleeding, emetics and the free administration of syrup of lemon (Lettre à M. le Baron de Breteuil, December, 1723), and thirty years later recommended him a stay at Plombières (Lettre à d'Argental, August 10, 1753).

In my paper at the recent Congress of the History of Medicine, at Geneva, on "Voltaire and English Doctors," I pointed out that though he suffered from various illnesses during his residence in London from 1726 to 1729, the name of the doctor who attended him was not known. Voltaire was personally acquainted with Cheselden, and probably with Sir Hans Sloane, Mead and Freind (whose death he describes in an English letter to Towne¹), as well as with other medical Fellows of the Royal Society (especially Arbuthnot and Pemberton), of which he was himself elected a Fellow in 1743. He seems to have had some knowledge of the works of Harvey, Sydenham and Freind, as well as of the medical essays in the *Philosophical Transactions*, from which, according to Lanson, he probably derived his knowledge of inoculation. In addition to Richard Mead, three other doctors, whose identity I have discussed in my previous paper, appear in the list of the English subscribers to the edition of *La Henriade*, published in London in 1728, viz., Misobin (probably John Misaubin), Brocksom (probably Noel Broxholme), and Chamberlain (possibly Hugh Chamberlen, Junior, the last of the celebrated obstetrical family).

Among the less-known doctors whose acquaintance Voltaire made in London was a certain Dr. Towne, the author of a work on the diseases most prevalent in the West Indies, who translated into English part of *La Henriade*. It is noteworthy that Tronchin, then a youth of 19, was in London at the same time as Voltaire, and even paid a visit to Bolingbroke, with whom Voltaire was closely associated, during his stay in London, but there is no record of Voltaire meeting Tronchin at this early date.

Jean Baptiste Sylva, first physician to the king, appears to have attended Voltaire in 1730, as Voltaire expresses his gratitude to him in the following graceful sextet accompanied by his portrait:—

Au temple d'Epidaure on offrait les images
Des humains conservés et guéris par les Dieux,
Sylva qui de la mort est le maître comme eux,
Mérite les mêmes hommages.
Esculape nouveau, mes jours sont tes bienfaits,
Et tu vois ton ouvrage en revoyant mes traits.

Sylva also figures in the list of the French writers in the *Siècle de Louis XIV*, where we read the following appreciation: "Sylva (Jean Baptiste), born at Bordeaux, a very celebrated doctor of Paris, and author of a famous book on bleeding; he was very superior to his book. He was one of the doctors whom Molière would not have dared to make ridiculous, even if he could. Born in 1684, died in 1740."

¹ "Voltaire, Montesquieu and Rousseau in England," by J. Churton Collins, 1906, p. 92.

A presentation copy of *La Henriade* to Sylva, with Voltaire's autograph, was formerly in possession of the late Sir William Osler ("The Life of Sir William Osler," by Harvey Cushing, 1925, i, p. 675).

On his visit to Leyden in 1737 Voltaire consulted Boerhaave, whose name frequently occurs in his writings, especially in connexion with chemistry (*Eléments de la Philosophie de Newton*, Chap. VII: *Essai sur la Nature du Feu*, Art. I and II; *Mémoire sur un Ouvrage de Physique: Défense de Newtonianisme; Siècle de Louis XIV*, Chap. XXXIV; *Dictionnaire Philosophique*, Art. Anatomie). During his stay at Cirey, when he was busily engaged in laboratory work, Voltaire wrote to his friends Abbé Moussinot (November, 1738) and Thieriot (December, 1738), for a French translation of the *Institutiones medicæ*. It may be said in passing that Tronchin was one of Boerhaave's most illustrious pupils. Another pupil of Boerhaave, van Swieten, provoked Voltaire's satire, partly because he was an opponent of inoculation, and partly because he was instrumental in forbidding the sale of Voltaire's books in Vienna (*De l'horrible Danger de la Lecture: Eptre au Roi de Danemark*).

During the Cirey period Voltaire had as his medical attendant a Dr. Valdruche, of whom nothing else is known beyond the fact that Voltaire sent the doctor's son with a note of recommendation to d'Argental (*Lettre à d'Argental*, November 3, 1738).

There is also a letter dated August 27, 1735, written from Cirey and addressed to a M——, whom Voltaire thanks for his prescription and his visit in the following words:—

"Your society seems to me to be as welcome as your advice. Happy are the sick who have you as their doctor and the healthy who have you as a friend."

During the Potsdam period he told Bagieu, a well-known Paris surgeon (December 19, 1752), whom he subsequently consulted about his relative Daumart (January 11, 1761), that Codenius, physician to the King of Prussia, had given him a very long German prescription which he threw into the fire without being any the worse for it. "He is a very good fellow," Voltaire continued, "and knows as much as the rest, and when he sees that my teeth are falling out and that I am suffering from scurvy, says that I have a scorbutic affection." It is possible also that Lieberkühn, who in addition to being an anatomist was also a court physician (*Histoire du docteur Akakia*, § vii; *Lettre à Frédéric II*, October 14, 1751), may have attended Voltaire during his stay at Potsdam.

It was during this period that Voltaire made the acquaintance of La Mettrie, but it is doubtful if he ever sought his advice, as he speaks of him as "the worst doctor in the world in practice though as well trained in theory as any of his confrères" (*Mémoires pour servir à la vie de M. de Voltaire*), and in a letter to Mme. Denis (November 6, 1750), after an allusion to La Mettrie's book, *L'Homme Machine*, he exclaims, "God save me from having him as my doctor. He would give me corrosive sublimate instead of rhubarb in the most innocent manner imaginable and then would burst out laughing!" Elsewhere (*Lettres à S. A. Mgr. le Prince de * * * sur Rabelais, etc.*, Lettre VII) he speaks of him as the best commentator of Boerhaave, and in a letter to Koenig (March 12, 1753) he says, "I admit that La Mettrie committed follies and wrote bad books, but in his smoke there were flashes of flame." His death from a surfeit of eagle pie disguised as venison is related in a letter to Mme. Denis (November 17, 1751).

Apart from Boerhaave, the most distinguished of all Voltaire's doctors was undoubtedly Tronchin, who is described in the *Correspondance* in the following flattering terms: "A man as wise as Aesculapius and as handsome as Apollo" (*Lettre à Mme. de Fontaine*, September 6, 1755; *Lettre à Mme. la Comtesse de Lutzelbourg*, August 12, 1756); "Apollo—Aesculapius—Tronchin" (*Lettre à Mme. de Fontaine*, March 17, 1756); "The Messiah Tronchin" (*Lettre à d'Argental*,

April 1, 1756); "The oracle of Geneva" (Lettre à Damilaville, May 28, 1765); "As upright a man as he is a good doctor" (Lettre à De Pezay, January 5, 1767); "The greatest physician in Europe and the only one who understands nature" (Lettre à Frédéric II, December, 1758).

Numerous references are made in the *Correspondance* to Tronchin's enormous practice. Writing to Richelieu on May 1, 1755, Voltaire says that people came from Lyons and Dijon to consult Tronchin, and four years later he tells Frederick the Great (May 19, 1759) that it would be impossible for Tronchin to visit Frederick's brother in Germany owing to the demand for him in France. From a letter to Damilaville (May 30, 1765) we learn that

"Tronchin is not free a minute, and that he cannot devote to his prodigious number of consultations the attention he would like."

Tronchin undoubtedly had more authority over Voltaire than any other of his medical advisers had. In particular, he had sufficient influence to check the patriarch's over-indulgence in coffee, of which he used to consume as much as twelve cups a day. During the last twenty years of his life he reduced his allowance to two or three cups which, by the doctor's advice, he mixed with chocolate.¹

Voltaire sought Tronchin's advice not only for himself but also on behalf of his friends, such as Frederick the Great (December, 1758), Mlle. Clairon (March 15, 1763), Damilaville (November 28, 1762, April 2, 1764, June 22, 1765), and his niece, Mme. de Fontaine (Lettre à Thieriot, October 14, 1756). On only a few occasions did Voltaire venture to criticize Tronchin, as in his treatment of Daumart (Lettre à Mme. de Fontaine, November 28, 1762; Lettre à Damilaville, December 6, 1768), and Mme. D'Argental (Lettre à D'Argental, August 9, 1757).

After Tronchin left Geneva for Paris in January, 1766, d'Argental asked Voltaire who would be his doctor, and received the reply, "No one, or the first comer" (Lettre à d'Argental, January 24, 1766).

In a footnote, however, to *La Guerre de Genève* (Chart III), written in 1768, Voltaire speaks of one Jori, who did much to bring about peace as "my ordinary medical attendant," and in the next year he writes to the Duc de Choiseul (July 16, 1769) the following characteristic letter on behalf of the local practitioner at Ferney:—

"Nothing is more fitting than the request of an old patient for a young doctor; nothing is more just than an increase in salary when work increases. My lord is well aware that formerly we only had scrofula in the deserts of Gex, and that since the troops have been there we have had something much worse. The old hermit, who, it is true, has not received either of these blessings from Providence, but who takes a sincere interest in all who are honoured by such gifts, takes the liberty of pointing out with sorrow and respect that our kind Dr. Coste, who intends to prevent us from dying, has not enough to keep himself alive, and in this respect is quite the reverse of the great doctors of Paris. He entreats my lord to take pity on a little country of which he is the only hope."

As the result of Voltaire's intercession Coste's salary was raised from 150 to 1,200 francs.

We find Voltaire corresponding with Bouvart, a leading practitioner of Paris, and professor at the Royal College of Medicine, whom he consults about his diet (March 5 and 26, 1770), and Tissot of Lausanne (Bengescu, *Bibliographie de Voltaire*, tom. iii, p. 352), whom, in one letter written in September, 1773, he invites to Ferney, and in the other, undated, he thanks for the gift of "Inoculation Justifiée," in which Tissot alludes to Voltaire's defence of inoculation in the *Lettres Philosophiques*. On his last visit to Paris in 1778, Voltaire sent for Tronchin, who after warning him that he was living on the capital of his strength, and that a tree of eighty-four could not be transplanted unless one wished to kill it, advised him to

¹ "Théodore Tronchin," by Henry Tronchin, 1906, p. 147.

return to Ferney as soon as possible, and even offered him his own carriage for this purpose. Voltaire was also visited during his last illness by the fashionable physician Lorri, whom the Marquis de Villette sent for owing to his dislike of Tronchin, but Lorri did not apparently continue his attendance (H. Tronchin, *loc. cit.*, p. 232).

Voltaire was far from being an ideal patient. Like Herbert Spencer, a hundred years later, he was too fond of arguing with his medical attendants and too little inclined to carry out their instructions. In a letter to d'Argental (November 6, 1767) he remarks that "it is a good thing to ask doctors' advice sometimes, provided one does not believe them blindly." In this respect he reminds us of his own description of Molière (*Vie de Molière*), whom Louis XIV once asked, "What does your doctor do for you?" "Sire," replied Molière, "we converse, he orders remedies, I do not take them, and I recover."

Other medical men with whom Voltaire corresponded, but without seeking their professional advice, were Haller (February 13, 1759), of whom he appears to have had a high opinion, though it was far from being reciprocated, Paulet, the author of several works on small-pox (April 22, 1768), and Pomme, the fashionable physician, and author of a work on the vapours (June 27, 1771).

Voltaire was acquainted with several medical men connected with the Court, such as Louvois' physician, La Ligerie, the inventor of the "Poudre des Chartreux" (*Siècle de Louis XIV*, Chap. XXVII); Marsolan, the medical attendant of the Duke of Orleans and of the Man in the Iron Mask (*Dictionnaire Philosophique*, Art. Anatomie; *Siècle de Louis XIV*, Chap. XXV); and Senac, first physician to the King, well known for his work on diseases of the heart, on whose kindness he told the Comte de Rochefort he could always rely (*Correspondance*, July 3, 1769). We find Voltaire consulting him about a contagious disease in the neighbourhood of Geneva (Lettre à M. Senac, December 6, 1760), which Rattel thinks was most probably a small outbreak of typhoid fever, and again about his relative Daumart, in 1769 (Lettre à Comte de Rochefort, *loc. cit.*).

In the paper read at the Geneva Congress, I remarked that among the many Englishmen who visited Voltaire at Ferney or elsewhere, three at least were medical men, namely, Oliver Goldsmith, Samuel Sharp and John Moore, all of whom have left on record an expression of their admiration for the patriarch.

Throughout Voltaire's work we find references to some of the masters of medicine, such as Hippocrates (*Dictionnaire Philosophique*, Arts. Anatomie, Livres; *Histoire du Dr. Akakia*; *L'A B C*, troisième entretien; *De l'Ame*; *Des Singularités de la Nature*, Chap. XXXV; *Discours de l'empereur Julien*; Lettre à Bagieu, April 10, 1752); Rhazes (Lettre à Paulet, April 22, 1768); Fernel (*Essai sur les Mœurs*, Chap. CLVIII; *Un Chrétien contre six Juifs*, XV); Servetus; (*Essai sur les Mœurs*, Chap. CXXXIII, CXXXIV; *Dictionnaire Philosophique*, Art. Arianisme, Arrêts de Mort); Harvey (*Essai sur les Mœurs*, Chap. CXXXIV; *L'Homme aux quarante écus*, Chap. VII; *Dialogues d'Euphémère*, neuvième entretien; *Articles extraits de la Gazette littéraire de l'Europe*, April 4, 1764); and Sydenham (*Dictionnaire Philosophique*, Arts. Fièvre; Livres; Lettre à Bagieu, April 10, 1752).

Voltaire told Paulet (*Correspondance*, April 29, 1768), that he had read more works on medicine than Don Quixote had on chivalry, but the medical work with which he was probably most familiar was that of Astruc on the Venereal Diseases, to which he frequently refers (*Dictionnaire Philosophique*, Arts. Job; Lèpre et Vérole; Livres; *La Bible enfin expliquée* (Lévitique)).

Numerous allusions are made to celebrated anatomists such as Bartolommeo Montagnana (*L'Homme aux quarante écus*, Chap. XI); Vesalius (*Essai sur les Mœurs*, Chap. CLVIII; *Dictionnaire Philosophique*, Art. Anatomie); Ruysch (*Anecdotes sur*

¹ In his correspondence Voltaire alludes to him as "old Stentor-Astruc" (Lettre à d'Alembert, August 13, 1760), and "Harpagon-Astruc" (Lettre à Marquis de Florian, March 12, 1766), in reference to his overbearing and avaricious habits.

Pierre Le Grand, Essai sur les Moeurs, Chap. CXLI); Winslow (*Dictionnaire Philosophique*, Art. Anatomie); Bartholin (*ibid.*, Art. Prépuce); and Vieussens (*ibid.*, Art. Anatomie).

In the short notices of the principal writers in the *Siècle de Louis XIV* we find eleven medical men mentioned, of whom the best known are Guy Patin, Hecquet, who is also alluded to in *Dictionnaire Philosophique* (Arts., Ventres paresseux, Viande), Théophraste Renaudot and Jean Baptiste Sylva, the others being Bernier, Charas, Helvétius, Méry, Naudé, Charles Patin and Perrault. Of these notices those on Guy Patin and his son Charles alone need detain us:—

"Patin (Guy), born at Houdai in 1601, physician more famous by his scurrilous letters than by his medicine. His collection of letters has been read with avidity, because they contain news and anecdotes which everyone likes, and satire which is still more welcome. He serves to show how contemporary authors who are in a hurry to report the news of the day are untrustworthy guides for history. The news is often false or disfigured by its malevolence; besides, this multitude of little facts is hardly of any value except to little minds. Died in 1672."

"Patin (Charles), born in Paris in 1693, son of Guy Patin. His works are read by scholars, and his father's Letters by the idle. Charles Patin, who was a very learned antiquary, left France and died, Professor of Medicine at Padua, in 1693."

Among the lesser luminaries in the medical world of whom Voltaire speaks are van Dale, the predecessor of Fontenelle, in his work on oracles (*Dictionnaire Philosophique*, Art. Oracles); Jean Paul Marat, whose book *De l'Homme* he scathingly reviews (Articles extraits du *Journal de Politique*); Garth, the author of *The Dispensary*, which he describes as superior to Boileau's *Lutrin* in imagination, variety and naiveté (*Dictionnaire Philosophique*, Arts. Bouffon; Caractère); Saint-André, Court anatomist to George I and dupe of Mrs. Tofts, the rabbit-breeder of Godalming (*Dictionnaire Philosophique*, Art. Ame, and *Singularités de la Nature*, Chap. XXI); and Poissonnier, who discovered the secret of making sea-water drinkable (*Précis du Siècle de Louis XV*, Chap. XLIII).

In the dental profession Voltaire makes special mention of L'Écluse, a surgeon dentist of Geneva, who attended his niece, Madame Denis, and describes him as "one superior in his art, a man of honour and highly esteemed" (*Lettre à Damilaville*, January 16, 1761).

Voltaire's interest in veterinary science is shown by his correspondence with Bourgelat, Director-General of the Royal Veterinary School, to whom on one occasion he sent the bladder of one of his oxen in which he had found numerous stones (October 26, 1771). In a subsequent letter to Bourgelat, dated March 18, 1775, he writes:—

"I am surprised to find that before you cattle were only the concern of butchers and that horses had only a blacksmith as their Hippocrates. Real help is wanting in the best administered countries. You have put an end to this disgraceful and dangerous state of affairs. . . . I should like a search to be made for remedies for the contagious diseases of our animals when they are in good health for use when they are ill. A dozen different remedies could then be tried on a hundred oxen attacked, and one might reasonably hope that some of the remedies would succeed. There is at the present time a contagious disease in Savoy, about a league from me My method of protection is to have no communication with the plague-stricken, to keep my animals scrupulously clean, in well-ventilated stables, and to give them wholesome food."

Voltaire's precautions against epizootics in his district are also illustrated in a letter recently brought to light by Vézinet,¹ in which he says:—

"The preservation of cattle being of the greatest importance in our unhappy country, I sent a message to Fretter, one of the butchers in Ferney, that if he did not bring a certificate

¹ "Autour de Voltaire," 1925, p. 34.

for the three oxen he bought about a fortnight ago I would expel him from Ferney. I had the same message sent to Abraham Meunier, who appears to be a very doubtful and dangerous character, capable of infecting the whole country in order to gain ten sous."

Voltaire's frequent association with apothecaries, due to his firm belief in the efficacy of drugs, especially cassia and rhubarb,¹ of which he always kept a store in his travelling medicine chest, is exemplified in the following passages from his correspondence. In a letter to Tollot (May 21, 1768) he thinks it necessary to emphasize the honourable status of the apothecary:—

"One can very well," he writes, "be a citizen of Geneva and an apothecary at the same time. My friend, M. Colladon, belongs to one of the oldest families in Geneva, and is one of the best druggists in Europe. When one writes to an apothecary in Germany, one addresses the letter to 'Monsieur N., very renowned apothecary.' MM. Geoffroi and Boulduc, who are apothecaries, belong to the Académie des Sciences and have been friends of mine all their life. All the great doctors of antiquity were apothecaries and compounded their remedies themselves, in which they were far superior to our doctors of the present day, many of whom do not know where the drug which they administer grows."

Writing to the Marquis de Richelieu (January 30, 1774), Voltaire asks to be recommended to the best apothecary in Bordeaux:—

"I have greater need of these gentlemen," he said, "than of all the kings in Europe. For nearly eighty years my fate has absolutely depended upon them."

Lastly, in a letter to the Marquis de Thibouville (March 7, 1776), he writes:—

"The sick old man was talking yesterday to an apothecary at Geneva. Alas! it is only too often that he has conversations of this kind. 'By the way,' said the sick man, 'what is barberry a cure for?' 'Nothing at all,' replied the apothecary, 'like most remedies.' 'And where do you get barberry lozenges?' continued the sick man. 'They are made at Dijon,' the apothecary replied. 'I happen to have a small box.' 'Send it to me at once,' said the sick man. He did so, and I am sending it on to you."

Voltaire's attitude to the medical profession as a whole can best be estimated from the following passages, which show his appreciation of their services to humanity.

In the *Dictionnaire Philosophique* (Art. Extrême), after showing that there is an art of warfare he continues,

"The same may be said of medicine, that art of operating with the hand and head to restore to life a man who is going to lose it. The first who bled and purged a man in an apoplectic fit at the right moment, the first who determined to plunge a knife into the bladder to extract a stone and close the wound, the first who could prevent gangrene in a part of the body, were doubtless divine and did not resemble Molière's doctors. Pass now from this obvious example to less striking and more equivocal cases; you see recoveries from fevers and diseases of all kinds without it being proved whether it was nature or the doctor who wrought the cure; you see diseases of which the issue cannot be foretold. Twenty doctors are mistaken about them; the one who has the most intelligence and the keenest insight divines the nature of the disease. There is therefore an art of medicine, and the best man knows its intricacies. Thus La Peyronie divined that a courtier must have swallowed a sharp bone which had caused a dangerous ulcer, and in this way Boerhaave guessed the cause of the unknown and cruel disease of a Count Vassenaar. There is therefore really an art of medicine, but in every art there is a Virgil and a Maevius."

In another passage in the *Dictionnaire Philosophique* (Art. Médecins) we read:—

"It is true that regimen is better than medicine. It is true that for a very long time out of a hundred doctors ninety-eight were charlatans. It is true that Molière was right in making fun of them. . . . It is none the less true that there are a hundred occasions on

¹ On his arrival at "Les Délices" he wrote to his Lyons banker, Robert Tronchin, first for "a large root of rhubarb capable of purging a province" (March 25, 1755), and then for 25 lb. of cassia (December 3, 1755) (H. Tronchin, *loc. cit.*, p. 148).

which a good doctor can save life and restore us the use of our limbs. If a man has an apoplectic stroke an infantry captain or a court councillor will not cure him. Cataracts form in my eyes and the lady next door will not remove them. I make no distinction here between the physician and surgeon : these two professions have long been inseparable."

The most laudatory passage, however, is to be found in the *Siècle de Louis XIV* (Chap. XXXIII), where, at the end of the chapter on the arts, Voltaire, who had previously (Chap. XXVII) described the successful operation performed by Félix on the king's fistula, pays the following tribute to French surgery and medicine :—

"After having reviewed all the arts which contribute to the delight of individuals and the glory of the State, let us not forget the most useful of all the arts, in which the French surpass all the nations of the world : I refer to surgery, in which the progress was so rapid and celebrated in this age that people came to Paris from the ends of Europe for all the cures and operations which required unusual dexterity. Not only were there hardly any outstanding surgeons except in France, but it was only in this country that the necessary instruments were brought to perfection. France supplied all the neighbouring countries with them, and I have it from the celebrated Cheselden, the greatest surgeon in London, that he was the first to have his instruments made in London in 1715."

Voltaire is doubtless expressing his own opinion in the following words, which he puts into the mouth of Dr. Akakia, concerning the proposal made by Maupertius that doctors should not be paid if their patients died :—

"I must be pardoned for disapproving of this writer treating his doctor as he does his booksellers. He wants to make us die of hunger. He does not want doctors to be paid when unfortunately the patient does not recover A doctor promises his attention and not a cure. He does all he can, and he is paid for that" (*Histoire du Docteur Akakia*).

The passages in which Voltaire indulges his satirical humour at the expense of the profession are relatively few in comparison with those in which he expresses his appreciation and gratitude, and, apart from the *Contes*, are mainly to be found in his correspondence, where his remarks are not to be taken too seriously. Thus, in a letter to Comte d'Argental (November 6, 1767), he says :—

"I did not know that you had buried your doctor. I know of nothing so ridiculous as a doctor who does not die of old age, and I cannot conceive how one can expect to obtain health from persons who cannot cure themselves. It is a good thing, however, to ask their advice sometimes, provided one does not believe them blindly."

In a similar vein he writes to Cideville (November 11, 1753) :—

"I only need doctors to finish me, but, thank God, I only see them for the pleasure of their conversation when they are intelligent, just as I see theologians, without believing in either."

In letters to Thieriot (July 12, 1765) and d'Argental (February 25, 1774) he says :—

"One can live and die without doctors," and in another letter to Thieriot (October 8, 1760) he writes, "As you are living with a doctor it is not surprising you are ill."

The frequently quoted saying, attributed to Voltaire, that "doctors are people who pour into bodies of which they know little drugs of which they know less," I have not been able to find in any of his works. Among the satirical passages relating to doctors which are to be found in the *Contes* the following, taken from *L'Ingenu* (Chap. XIX), deserves to be quoted :—

"A neighbouring doctor was at once sent for. He was one of those who visit their patients in a hurry, who mistake the case they are attending for the one they have just seen, and who blindly practise a science which is not devoid of uncertainty and danger even when the doctor possesses a sane and mature judgment. He made the disease twice as bad by his haste to prescribe a fashionable remedy. Fashion in medicine! This absurd idea was too common in Paris."

While, on the whole, Voltaire had a due respect for regular practitioners, he was scathing in his denunciation of quacks and quack remedies. Among the many quacks mentioned in his works the most flagrant was the notorious Swiss uromantist, named Schuppach, who enjoyed an immense vogue among the French nobility. In a letter to De Lisle (April 18, 1774) he describes him as the rankest charlatan that has ever existed, and in a letter to the Marquis de Florian (January 3, 1794) he says that the ridiculous charlatanism of divining diseases and temperaments by the urine is an outrage on medicine and reason. Again, in the *Histoire de Jenni* (Chap. IX) he illustrates the pretentiousness of this quack by saying:—

"There is no one who can retain in his memory the list of all the diseases which beset us, and yet the Swiss urine doctor claims to cure them all."

Other quacks mentioned by Voltaire are Villars, who sold a nostrum which he claimed would make man live 150 years, though it consisted merely of Seine water and a little nitre (*Dictionnaire Philosophique*, Art. Charlatan); the Chevalier Taylor (*Homélie du Pasteur Bourn*), Bougros, a guardsman, who was in turn surgeon, physician and apothecary, and was accused of having poisoned his mistress (*Lettre à M. Hennin*, March 16, 1770); and a druggist at Geneva who attempted to cure *gutta serena* by electricity (*Lettre à Mme. de Deffand*, June 5, 1772).

Voltaire was doubtless alluding to Nicolas Andry, sometimes known as *homo verminosus*, who was editor of the *Journal des Savants* and author of a work on helminthology, when he says (*La Bible enfin expliquée—Lévitique*):—

"We have had several charlatans who have maintained that all diseases were due to worms, and that as each kind of animal was devoured by another kind, one might have the worms of apoplexy and epilepsy devoured by anti-apoplectic and anti-epileptic worms. What a large number of charlatans there are."

Among the principal quack remedies in vogue at the time of which Voltaire speaks were potable gold, which he describes as a "swindle and a rogue's trick to deceive the people" (*Dictionnaire Philosophique*, Art. Fonte); Le Lièvre's balm of life (*Lettre à Thieriot*, September 15, 1768; *Dictionnaire Philosophique*, Arts. Almanach, Catechisme, Chinois, Maladie-Médecine); Arnould's sachets, which were worn round the neck and supposed to cure epilepsy; and Kayser's pills,¹ which were vaunted as a remedy against syphilis (*Lettre à Hume*, October 24, 1766; *Dictionnaire Philosophique*, Art. Almanach).

Many superstitious and erroneous doctrines connected with normal and morbid processes are mentioned by Voltaire. Chief among these was the doctrine of spontaneous generation which was upheld by the Jesuit Needham and disproved by the Abbé Spallanzani, to which repeated allusions are made (*Dictionnaire Philosophique*, Art. Dieu, Génération; *Questions sur les miracles*, Lettres IV and V; *Des Singularités de la Nature*, Chap. XX; *La Défense de mon oncle*, Chap. XIX; *L'homme aux quarante écus*, Chap. VI; *Histoire de Jenni*, Chap. IV; *Correspondance*, Lettres au Marquis de Villevielle, August 16, 1768, De Lisle de Sales, November 25, 1770, Abbé Spallanzani, March, 1776, June 6, 1776).

In a letter to Spallanzani (March 1776) Voltaire says:—

"I have read your instruction book with much pleasure. You have given the last blow to the eels of the Jesuit Needham. They wriggle in vain, they are dead, and Bonnet will not revive them in his *Palingénésie*."

Elsewhere (*Dictionnaire Philosophique*, Art. Génération) he writes:—

"No animal and no vegetable can be formed without a germ, otherwise a carp might grow on a yew tree and a rabbit at the bottom of a river."

¹ See P. Delaunay, "Le monde médical parisien au dix-huitième siècle," 2e édition, 1906, pp. 243-45.

Among other superstitions to which Voltaire refers are the influence of the moon on menstruation and on the crisis in fevers, and of the tides of the ocean on death (*Dictionnaire Philosophique*, Art. Influence) ; the cure of paralysis by eels (*ibid.*, Art. Préjugés), and of epilepsy by the fat of a man who had been hanged (*ibid.*, Art. Supplices) ; and the method of treatment *per accubitus junioris* (*Essai sur les mœurs*, Chap. LI and CXCVII). "These ideas," says he, "and a thousand others have been the errors of charlatans in days gone by, who judged without reasoning, and after being deceived themselves, deceived others (*Dictionnaire Philosophique*, Art. Préjugés).

Section of the History of Medicine.

President—Dr. J. D. ROLLESTON.

Assyrian Medical Texts.

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II.

SINCE the publication of my *Assyrian Medical Texts* I have made some sixty-nine joins from the fragments therein.¹ These will be noted in their proper places in the translations: those which affect translations already published in *PRSM*. 1924 are *AM*. 1, 4 (K. 2615, No. 3) + 99, 2 (K. 2448 +

¹ To Herr Ebeling must be given the credit of noting one other in his *Keilschr. Medicinischen Inhalts* (K. 3267 + 9438, my *AM*. 26, 2 and 26, 8), and another which I regrettably omitted, in incorporating in *AM*., to acknowledge.

It will be seen that many of the vegetable drugs have been translated without comment, and for these the reader is referred to my *Assyrian Herbal* (Luzac & Co.). I must here record my thanks to Professor S. Langdon for the ever-ready way in which he has put his library, as well as his notes for his forthcoming Sumerian Dictionary, at my disposal.

The abbreviations used herein are: *ADD.*, Johns, *Assyrian Deeds and Documents*; *AH.*, my *Assyrian Herbal*; *AJSL.*, *American Journal of Semitic Languages*; *AM.*, my *Assyrian Medical Texts*; *ASKT.*, Haupt, *Assyr.-Sumer. Keilschrifttexte*; *Br.*, Brünnow, *List of Cuneiform Ideographs*; *BSGW.*, *Berichte u. d. Verh. d. kgl. Sächs. Gesellsch. d. Wissenschaften*; *CT.*, *Cuneiform Texts from Babylonian Tablets*; *Del.*, *HWB.*, Delitzsch, *Handwörterbuch*; *Diosc.*, Dioscorides, ed. Sprengel; *E.*, Ebeling, in *Archiv für Geschichte der Medizin*; *EB.*, *Encyclopædia Britannica*, 11th ed.; *Holma*, Holma, *Körperteile*; *Hrozný*, *Getr.*, Hrozný, *Das Getreide im alten Babylonien*; *IB.*, Ibn Beithar, in Leclerc, *Notices des Manuscrits*, xxiii, xxv, xxvi; *KAR.*, Ebeling, *Keilschrifttexte aus Assur, Religiösen Inhalts*; *KB.*, Schrader, *Keilinschriftliche Bibliothek*; *Kü.*, Küchler, *Beitr. z. K. d. Assyr.-Bab. Medizin* (I = K. 191, II = K. 71b, III = K. 61); *MA.*, Muss-Arnolt, *Assyrian Dictionary*; *OLZ.*, *Orientalistische Literaturzeitung*; *P.*, Squire, *Companion to the British Pharmacopæia*, 18th ed., 1908; *PBE.*, *Babylonian Expedition of Pennsylvania*; *PC.*, *Penny Cyclopædia*; *Pliny*, *Natural History* (ed. Bostock); *PRSM.*, *Proceedings of the Royal Society of Medicine*; *PSBA.*, *Proceedings of the Society of Biblical Archaeology*; *R.*, Rawlinson, *Cuneiform Inscriptions of Western Asia*; *RA.*, *Revue d'Assyriologie*; *SAI.*, Meissner, *Seltene Assyrische Ideogramme*; *SM.*, Budge, *Syriac Book of Medicines*; *ZA.*, *Zeitschrift für Assyriologie*; *ZK.*, *Zeitschrift für Keilschriftforschung*.

Numbers, such as 21, 1, 1, or *AM*. 21, 1, 1, refer to page and tablet-number and line in *AM*.

An asterisk * affixed to a drug means that there is a very slight doubt about the exact species, or, a slight variability possible, owing to there being a closely allied and almost interchangeable candidate for the same drug-name; **, some doubt about the identification, but good reason for it; a query (?), when there is real and justifiable doubt.

6386); *AM.* 2, 1 (K. 2491 + 8356, No. 4) + *CT.* xxiii (K. 2354, pl. 23 ff., a join, not a duplicate); *AM.* 3, 5 (K. 6224, No. 8) + 17, 1 (K. 6560, No. 49); *AM.* 6, 3 (K. 9828 + 11868, No. 22) + *CT.* xxiii (K. 2354, pl. 23 ff.); *AM.* 6, 9 (K. 10212, No. 24) + 2, 2 (K. 13884); *AM.* 8, 1 (K. 10891, now joined to K. 2573, No. 26).

It is probable that *AM.* 8, 1 (No. 26) belongs to a series which deals entirely with eyes, of which the title is *Šumma amelu* [ênâ^{II}-šu] . . . "If a man's eyes] . . ." (*AM.* 12, 7). *AM.* 8, 1, is followed in the series by *AM.* 16, 1. Another tablet is *AM.* 12, 7, followed by *AM.* 12, 4. Unfortunately little more is known, although *KAR.* 202 gives a catch-line which may belong (*Šumma amelu* ênâ^{II}-šu GIŠ.MI AR-ma, etc.).

I am greatly indebted to Dr. H. R. Hall, Mr. Sidney Smith, and Mr. C. J. Gadd for much courtesy in furthering the work on these texts.

TRANSLATIONS.

B. DISEASES OF THE EYES (*continued*).

No. 28, A. *AM.* 11, 2 (K. 2440, etc.). To this I am now strongly inclined to think that No. 27, *AM.* 8, 2 (K. 10495) must be added, although there is no "join". To *AM.* 10, 3 (rev. of K. 2440) must probably be added K. 6425 (*AM.* 13, 6), although there is no actual contact. These are thus included:—

Obverse. 1. (If ditto, *storax, *Solanum* . . .) [in] oil thou shalt put, apply with thy finger. (If ditto, the head of a lizard thou shalt dry . . .), ditto, of a lizard of the wall thou shalt dry, bray, in a copper pan¹ (?) thou shalt put on the fire, apply.

3. (Thou shalt reduce *Kak ti ti lu*² . . .), for three days during the night (?) to her eye (?)³ continuously thou shalt apply.

4. (If a man's eyes ditto, and . . .) thou shalt mix in oil (and) pour into his eyes.⁴

5. (The brain of a *kultim*⁵ . . .) [in] oil, and the brain of a male dove (in equal parts thou shalt mix) and . . . continuously put in his eyes.

¹ ŠU.MULU "hand of a man"; cf. 19, 6, 13, and 𒍪𒍪 as "pan" (but doubtful; it may be some copper ingredient).

² *Kak-ti*, Boissier, *Div.* 103 and 107, part of body. There is a right and left *k*, it may be like *kibirru*, or black: the verbs used of it are *GAM-at* and *MAR-at*.

³ *Mu ša ši* clear on tablet.

⁴ Cf. 13, 6, 6, and 16.

⁵ For the brains of small animals in medicine, cf. *SM.* ii, 701, 704.

7. (A raven's egg¹ . . .) thou shalt take out and smear a copper instrument with curd . . . wash thy hands in water . . . [in] curd thou shalt mix² (and) apply.

10. . . . thou shalt apply³ continuously.

11. . . . thou shalt bray (and) apply.

12. . . . *tarḥu*-plant, one quarter (of a shekel) of mercury thou shalt bray (and) apply.

13. . . . one *bur*(?) flour of *ḥiṣpā*(?)⁴ in oil of cedar thou shalt bray (and) apply.

14. . . . *Solanum* thou shalt bray, in oil in a copper basin thou shalt beat up (and) apply.

15. . . . chamomile(?), *mint together thou shalt bray (and) apply.


16. . . . in oil thou shalt bray (and) apply.

17. . . . into his eyes thou shalt pour.

18. (?) . . . with water of alkali thou shalt wash his eyes.

20. . . . (and) 5 shekels of cantharides(?) in equal parts thou shalt mix . . . needle(s) of antimony in oil and copper-dust⁵ thou shalt bray (and) apply.

¹ Cf. S.M. ii, 663. I have to thank Mr. Sidney Smith for his correction in *Journ. Eg. Arch.*, 1924, 180.

² *Tulabak*. This root occurs also 41, 1, iv, 20, *ina bi tu-la-bak*; ib., 36, 37, *ina na-ku-a-ri ša mēl tu-la-bak*; and 19, 6, 9, "nine drugs *ša napsalti lu-ub-ki*." The Arab *labaka* "mix" gives a good comparison; Kū. 78 compared . The meaning is rather different in HAR vi-ku i-lab-bi-ku (55, 1, 3; 86, 3, 8?); *enuma sa.MURUB lu-ub-bu-ki (ka)* (56, 1 r. 10; 69, 8, 15); . . . *asḏāte lu-ub-bu-ka* (56, 1 r. 5), where it applies to a derangement of various internal organs.

The other word for "mix", *rabaku*, should be discussed here, as a noun occurs spelt *rib-ki* capable of being read *lab-ki*. *Tarbak*, common, was settled by Kū. 103 (occurring 4, 5, 6; 14, 1, 7; 15, 3, 15; 15, 6, 10; 16, 1, 1; 17, 6, 2; 20, 1, 8; 22, 2 r. 13; 39, 4, 1; 45, 4, 4; 50, 3, 10; 100, 3 r. 14; etc.) from the Heb. *rābak*. *Ribku*, translated perhaps unnecessarily closely *Gebäck* by E. (xiii, 9) in K. 8347 (my 45, 4), means simply "mixture" (11, 2, 27; 15, 3 r. 6, 9 bis; 15, 5, 9; 16, 3, 15; 19, 6, 6, 11; 21, 3, 3; 24, 1, 2; 37, 5, 8; 45, 4, 4; 49, 6 r. 9; 51, 10, 3; 61, 1, 13; 65, 1, 2; 76, 3, 5 = 82, 2, 14 r. 11; etc.). It is used frequently in the phrase *kima ribki tarbak*; but *ribku ša ʿnā*¹¹ "mixture for the eyes" (19, 6, 6, 11). An alternative is *rabiku*: *kima rabiki tarbak* (40, 5, 12; 50, 3, 10; 52, 3, 8; 53, 9, 3; 61, 2, 7; 68, 1 r. 10, 18; 80, 1, 6).

³ On this as "einreiben", see E. xiv, 35, and *Proceedings*, loc. cit., 4.

⁴ Cf. *ḥiṣpi ša giṣpi* ŠAR, CT. xiv, 50, 13.

⁵ It is unnecessary to point out the use of copper for ophthalmia.

22. . . . in a basin thou shalt cool, in a copper basin thou shalt mix, . . . of the copper basin thou shalt make an extract¹ (and) apply for seven days.

24. . . . pounded² [roses(?)], fat . . . antimony thou shalt bray, apply, and there shall be an assuaging³ of his eyes.

26. . . . *Lolium* cooled in a well thou shalt take and . . . thou shalt bray old(?) (or "burnt"?) copper⁴ in curd, as a mixture to his eyes thou shalt apply, and he will recover.

28. . . . *Bellis*, water of **Arnoglosson*, water of *Solanum*, . . . thou shalt take (and) in copper-dust (v. water of *Lolium*) thou shalt bray (and) apply to his eyes.

30. . . . thou shalt reduce, pound,⁵ bray in copper-dust, apply.

31. . . . thou shalt bury,⁶ take out, and bray in copper-dust (and) apply.

32. . . . thou shalt bray in copper-dust (and) apply.

33. . . . [the young of a raven], their eyes thou shalt put out with a dagger⁷; . . . the plants which the raven has brought to its young . . . its . . . thou shalt bray (and) apply.⁸

¹ *Tašammaš*, *ܬܫܡܡܫ* extraxit.

² *Pa'zute*, of roses (*AM.* 80, 1, 5, see *AH.* 85), for *pa'zute*; *E.* xiii, 10.

³ *pa* = *pašahu*.

⁴ For *ee* = "roasted, burnt," see No. 35, 5. "Burnt copper," so frequently used for eyes in *SM.* (ii, 88 ff.) (*ܢܫܥܐ ܕܝܫܥܐ*), is the "flower of copper" or "copper scale" of Pliny (*NH.* xxxiv, 24), procured by fusing copper, i.e. copper oxide (Roscoe, *Treatise on Chemistry*, ii, 421). On the other hand, we have "copper dust" frequently, which looks much like this "copper scale"; and *Kū.* may well have been right (iii, ii, 13) in seeing in it "old copper" especially as he quotes ii *R.* 30, 41, *URUDU.KAK.KU.E* = *erū ee ša kaḫḫaru ikušū*, "old copper which the earth has eaten" (cf. Pliny, *NH.* xxxiv, 20).

⁵ *Ta-pa-a-a[š]*, *E.* xiii, 9.

⁶ *Tetimmir*, *Del.*, *HWB.* 710; cf. 101, 2, iii, 3, *ina bit papaḫi tetimmir*, and *KAR.* No. 62 r. 14, *ina nāri tetimmir*.

⁷ *ŠI.KAK* = *šukurru*, in Zimmern, *Šurpu*, iii, 28, parallel to *paṭri šiparri*; cf. Thureau-Dangin, *Une Relation*, 6, n. 2, where a mountain is compared to *šelut šukurri*, and further on, l. 378, 96 š. of silver are included in booty, and also in l. 393, 1514 š. of *erī dannāti ḫallute* and *šelut š. erī dannāte*. See also Holma, *WB.* 5-6. *ܫܟܪܝܬܐ* is a dialect word for a kind of dagger. *šukurri* might perhaps be *śāyapī*, the Persian dagger (Xen., *Anab.* 4, 4, etc.).

⁸ The recipe is similar to *SM.* ii, 662: "for darkness of the eyes. Take a young swallow and dig out its eyes, and tie a mark to it and let it remain in its nest for three days. When its mother cometh and seeth that it is blind, it will go and bring a certain root and put it on its eyes and they will be opened."

36. . . . *kankadu*-plant thou shalt bray, on the GIG-GIR¹ of his eyelids² [thou shalt place] . . .³, pith of a reed, seed of *talupadi*-plant, . . . of the left (?) which has borne twins, . . . barley-flour, gazelle-dung (?)⁴ in a washing-basin thou shalt knead (?)⁵, . . . safflower-seed thou shalt roast, **Arnoglosson*. seed . . . [in] milk (?) together thou shalt bray, mix, in hot⁶ attar of roses [thou shalt knead and apply] for fifteen days. **Storax* for three days thou shalt apply.

43. . . . thou shalt bray, thou shalt blow into his eyes by a reed-tube.⁷

44. . . . in oil thou shalt bray, apply: "Akkadian salt". . .

45. (*Dup. of No. 26, 8.*)

Reverse. No. 28, B. *AM.* 13, 6 (K. 6425 + 6652) (*probably upper part of K. 2440, rev.*).

1. . . . to his eyes three times curd thou shalt bray, apply.

2. . . . [juice (tops)] of tamarisk, juice (tops) of laurel . . . [into] his eyes thou shalt squeeze.⁸

4. . . . thou shalt reduce, bray, apply.

5. . . . thou shalt bray, apply.

6. . . . honey, curd into his eyes thou shalt pour.

7. . . . wind goes not forth(?), . . . in honey thou shalt mix, apply.

9. . . . thou shalt weigh(?), apply.

10. . . . dry in curd thou shalt mix, ditto.

¹ GIG-GIR occurs Virolleaud, *Babyl.* i, 7, 79, "If GIG-GIR *ina kaḫḫad ameli šakin*." From the GIG it is some sickness; it might be "wen" or "pustule".

² *Huppi éná II-šu*; so read from *KAR.* 182 r. 10, *ḥu-up-pat éná II-šu*. Cf. also *ḥu-up-ti éná II*, No. 60 (*AM.* 94, 8, 22). See Holma, 17. Is it from חֶבֶד "edge, rim"?

³ . . . *kiki kuppute*.

⁴ LA, properly "rind" or "shell", *AH.* 279.

⁵ *Ta-gal-lu-[ul?]*, from גָּלַל "to roll"? Cf. 13, 6, 9, and 36, 1, 7, for *gal*. It can hardly be *ta-ḫal-lu* "thou shalt roast" (cf. l. 40).

⁶ *Sikruti* (= "distilled"?), see No. 35, 5.

⁷ GI.SAG.TAR; see Thureau-Dangin, *RA.* 1920, 102; E. xiii, 12, n. 2. See also *AM.* 24, 4, 13; 26, 4, 4, 5; 27, 10, 9; 31, 5, 6, 7; 34, 5, 9; 35, 2, 5; 36, 1, 7, 13; 38, 4, ii, 8; 45, 2, 5; 55, 3, 8; 64, 1, 10; 81, 1, ii, 19; 81, 8, 12.

⁸ *Tamaša*, טָמָשָׁה "press out", or *tamaza*, with the same meaning (*HWB.* 396).

11. . . . **Ricinus*(?),¹ green thou shalt wash in water, pound; their water . . . thou shalt make to issue; the effluence² (and) copper dust in equal parts thou shalt mix, bray in . . . and mountain honey, apply.

13. . . . in harlot's³ milk in equal parts thou shalt mix, bray, apply.

14. . . . thou shalt pour their water into a *burzu*-pot, . . . and take out, in copper dust (and) curd thou shalt bray, apply.

16. . . . [into] his eyes thou shalt pour, fat in copper-dust thou shalt bray, apply.

17. . . . and nettles in a stone mortar(?)⁴ thou shalt bray; to the middle of his eyes[thou shalt apply] . . . magnetic oxide of iron,⁵ root of male palm, . . . alum(?), separately(?)⁶ thou shalt bray, apply.

20. . . . fruit of poppy thou shalt pound, bray in oil, apply.

21. . . . alum(?), curd, ditto.

(The remainder, K. 2440, rev., *AM.* 10, 3, is much mutilated. For l. 2, cf. obv., l. 33; for l. 5, cf. obv., l. 17; l. 32, " *storax and nettle-seed.")

No. 28, C. *AM.* 15, 4 (K. 13393) (*perhaps part of K. 2440; dup. (?)*
No. 26, a-e ?).

1. . . . cantharides(?), fat of "Long"-bone of . . .

2. Sulphide of arsenic thou shalt bray, through a re[ed tube thou shalt blow] . . .

3. Thou shalt bind wool-cardings(?)⁷ to his head, ten *bur* of oil . . .
[This] for three days thou shalt do; lolium . . .

¹ **Bani-aši*. Is this **AG.UD*, **ricinus* (cf. *Br.* 2775 and 7779) ?

² *Šihiltu* שִׁחִילְתּוּ.

³ I cannot help thinking that *šamka*, as used in this connexion in the Medical Texts, means nothing more than "woman" simply; *SM.* is insistent in its parallel use of "woman's milk" without any ulterior meaning. Indeed, the parallel word *šarimtu*, which gets the meaning of "harlot" (see, e.g., *KB.* vi, 1, 375), may well be merely the Arab حُرْمَة (presuming that in this instance *h* = ح, as it apparently does sometimes). In the older edition of the *Gilgamish* Legend the form *šamkatu* takes the place of the later *šamḫatu*; it may be that the words are really not the same, and, recognizing the curious apparent inconsistency in the initials *š* or *s* in Assyrian, we may not be wrong in seeing the Syr. *accubans, conviva*, in *šamkatu*.

⁴ *takBAR.DU.E*, probably the same as *takBAR.DU.A*, *CT.* xviii, 32, iii-iv, 22, *mi-sil* (?) -*tum*.

⁵ See my *On the Chemistry*, 124.

⁶ *Ahé*, also 96, l. 4, in a similar connexion. Is it for *Aḫi-enna* ?

⁷ *Kunšam*, see *AH.* 43. Meissner, *Bab. Ass.* i, 254, "Knael."

5. If a man's eyes hurt, the buds of green (?) corn . . . , arsenic, *tuška*¹
 . . . -stone . . .

7. If a man's eyes hurt, ten *bur* . . . his temples(?)

No. 29. *AM.* 8, 3 (79-7-8, 156) (probably part of *K.* 2570, No. 26; *top broken*).

2. . . . thou shalt spin separately (two kinds of threads), thou shalt bind it on his temples.

4. . . . and hath no eye. Recite the Charm !

5. . . . of his right [eye ?].

6. . . . *ra aš ta ma at ra aš*. Recite the Charm !

7. . . . of his left [eye ?].

8. [Incantation for the Sick Eye ?]. Do as before.

9. . . . a basin thou shalt set, . . . shall say . . .

No. 30. *AM.* 8, 4 (*K.* 11803), *top broken*.

1. If ditto, flour(?) . . .

2. If a man's eyes . . .

3. If in his glance . . . For his recovery, one shekel of . . .

5. If a man's eyes will not . . .

6. **Storax*, stone of . . .

7. If a man's eyes . . . seven days in . . .

8. If a man's eyes . . .

No. 31. *AM.* 8, 5 (*K.* 13719), *top broken*.

1. . . . *cantharides*(?) . . . thou shalt apply to his eyes.

3. . . . *tamarisk* . . . *Nigella* . . . thou shalt wash his eyes . . . *antimony*-*needle*, thou shalt not take off.

7. . . . *asa foetida*, *Lolium* . . . thou shalt knead, bind on.

¹ Cf. (?) *tuskā*, Virolleaud, *Babyloniaca*, iii, 221: my *Chemistry*, 30.

9. . . . his eye . . . "salt of Akkad," . . . thou shalt bray . . . (as much as) seems good to thee¹ . . . thou shalt apply to his eyes, and he will recover.

14. . . . UMUN.PA.E (v. green *ḫutra*) . . . (it is) the Hand of Ishtar² . . . thou shalt put on the fire . . . apply, and he will recover.

No. 32. *AM.* 8, 6 (K. 10892), *top broken*.

2. . . . his head thou shalt shave . . . , bray [needle(s)] of antimony, apply, wash off in water, roses on his eyes [thou shalt bind].

4. . . . water(?) of mountain-honey in curd thou shalt mix [and apply].

5. [If a man's eyes] are affected, and *šišitu*³ comes over the pupil of his eyes . . . gum of **Pinus Halepensis*,⁴ *Lepidium*, seed of . . .

No. 33. *AM.* 8, 7 (S. 1308), *top broken*.

1. . . . [in] curd thou shalt bray, three times in one month thou shalt apply: cantharides(?) in curd thou shalt bray, apply . . . [in *mulu*]-*tinna*⁵

¹ *Riś-ka ukal*. Jastrow (*Trans. Coll. Phys. Phil.*, 1913, 370, l. 4) had the correct reading, but his translation for "thy aching head" is incorrect. Ebeling (*Arch.* xiii, 143, *CT.* xxiii, 13, iv, 13) "(das) genügt (?) dir" is probably right. The phrase occurs *CT.* xxiii, 33, 12-13, *tatar-ma tupašā taḥašal tašahāl riś-ka ukal ina libbi ½ ḫa teliḫki* "thou shalt dry it again and grind and strain (as much as) seems good to thee (?): therein thou shalt take ½ *ka*"; *AM.* 41, 1, iv, 29-30, "these eighteen drugs (with) one *kisal* (i.e. *bur*) of oil and cypress-oil thou shalt crush *riś-ka ukal* . . . (as much as) seems good to thee (?)." Cf. also 4, 5, 2 (duplicate of *CT.* xxiii, 13, 11-17); 65, 5, 6; 94, 9, 2. The phrase is paralleled in *mukil gaggadišu*, and *mukil riś limutti*, see *MA.* 380.

² For one form of "the Hand of Ishtar" = mania, see *JRAS.* 1924, 452.

³ *Šišitu* or *šilimtu* also on 13, 7, 3, of the eyes. The problem is to settle whether this is the *šišitu* of Holma, 104 ff., "womb," or whether he is wrong in his translation. "Womb" is obviously impossible here. *CT.* xiv, 3, i-ii, 17-19, give *ri-e-mu* = *ru-ub-šu*, *i-pu* = *i-ba-ḫu*, *ši-ši-tu* = ,, for all of which (with another, *šilitu*) Holma gives the meaning "womb".

But *rubšu*, besides its probable equivalence with رُبْش "mother", and مَرْحَل "womb" (as he shows), has an undoubted value "dung" (cf. Langdon, *Bab. Wisdom*, 47, l. 41, quoting *BE.* 31, 74, 42). In *AM.* this meaning is found, of asses, 15, 3 r. 12; 30, 1 r. 1; 99, 3 r. 10; of oxen, 13, 1, 5; 31, 2 r. 6, with urine of an ox, l. 5; *KIL.* 83, 1 r. 10, with *A.GAR.GAR* of a gazelle; of dogs and pigs, *epir ru-bu-uš kalbi epir ru-bu-uš šahī*, 98, 3, 17. (*A.GAR.GAR* is used for gazelle *passim*, and sheep, 69, 8, 8, the similarity of their dung being obvious. *KU* is used of a lizard, 8, 1, 29, and also of pig, 1, 2, 17; 103, 18.)

He quotes Boissier, *Choix*, i, 85 ff., *šumma ba-mat marti ša imitti (šumeli) ši-ši-tum a-rim*, and 92, *šumma irru saḫirāti éná v-šu-nu ši-ši-tum ar-mu*; and *CT.* xx, 6, Sm. 1412, 9-11, *šumma GIR 2-ma elû (šaplu) ši-ši-tu a-rim*. Hardly "womb" here. *TE* = *šišitu*, *CT.* xii, 11, 12a. Can it be connected with שִׁשִּׁית "glass" (i.e. a film) or גִּלְגִּל "glue" (improbable, but cf. *SM.* i, 91, l. i)? Or is it the (white) spot which occurs in the pupil?

⁴ Or perhaps opium. The text is broken.

⁵ *BI.MULU.TIN.NA* (10 *th.* in *AM.*), *MULU.BI.TIN.NA* (1, perhaps 2 *th.*, 45, 5, 4; 89, 4 r. 6?). Drunk in prescriptions 36, 2, 7; 66, 11, 13; 67, 1, 7. Cf. *ina taḥ-ri-iš MULU.TIN.NA šu*, 4, 5, 3 (duplicate of *CT.* xxiii, 13, 11-17): ½ *ka mi pa MULU.TIN.NA*, 41, 1, iv, 20.

[beer] thou shalt knead, bind on his eyes: *storax, *Salicornia*-alkali, **Ricinus* (?), without a meal . . .

3. . . . "salt of Akkad," *sikti*¹ of roast corn thou shalt mix(?) . . .

4. . . . copper in anointing-fat² [thou shalt apply] . . .

No. 34. *AM.* 9, 6 (K. 16459): must be dupl. Kü. iii, iv, 5. L. 2, perhaps "yellow rheum in the eyes"; cf. No. 39. L. 4, MUŠ.DIM.GURIN. [NA], used for teeth in three out of the four instances in *AM.* (28, 1, 1; 30, 3, ii, 5; 105, 1, 15), and here for eyes. In Kü. iii, iv, 6, the epithet *ritkubati* is applied to it, and (ib. 25) there is a "large *m.*" and (26) a "large *m.* of the desert". In 105, 1, 15, "If a man's tooth on the right side troubles him . . . the *m.* which run about the desert on his tooth he shall chew, gum of *galbanum thou shalt put in his left ear." If it were not for the sign MUŠ which rather points to a snake or similar, I should have suggested the lady-bird. Mr. Sidney Smith tells me that he remembers seeing one in S. Babylonia; I have seen them in quantities inhabiting the low bushes in the Anatolian hills (see my *Pilgrim's Scrip.*, 256), where it may be said definitely that they prefer to walk rather than fly. The lady-bird is particularly quoted for toothache in Fernie, *Herbal Simples*, 392, owing to a fluid which it secretes from its legs. On the other hand, *AM.* 28, 1, 2, seems to speak of the UD ša libbi-šu.

No. 35. *AM.* 10, 4 (K. 11695).

2. [If from a man's eyes blood has dropped(?)]³ and has stopped, the gall of a male sheep, the fat of . . . , **Ricinus* thou shalt bray in curd (and) apply . . .

4. [If from a man's eyes] blood has dropped(?) and has stopped, myrrh in . . .

5. [If a man . . . and] his eyes are troubled with blood dropping, *ammi . . . , alum, tannin, together thou shalt rub . . . thou shalt wash(?)⁴ knead, roast in an oven⁵ . . .

¹ *Sikti*, applied to parched corn here, and in 31, 4, 9 "15 šē si-ik-ti 'ašagi 15 šē sik-[ti]" (cf. 44, 5, 6): *zir epitati si-ik-ti* (13, 2 r. 10): *si-ik-ti 'šu.* . . . (34, 1, 24), and *saḫlē si-ka-a-ti* (39, 1, 33), *si-ki-te* (81, 1, 4), [*saḫlē*] ŠAR BIL¹ *si-ku-ti* (75, 1, 31) (Ebeling, xiii, 11, "perhaps perfumed mustard (?)") whatever drug that may be.

² *Sāki*, also 23, 10, 6. The root 𐎶𐎵𐎶 "anoint" is found in Zimmern, *Rit.* 26, i, 24, *i-su-ak*.

³ *Ifri*, and 1, 5, *ti-ri*, 𐎶𐎶𐎵 (unless this latter be the Heb. צרה).

⁴ Or "KA.LUH, *asa foetida*?"

⁵ *Ina*? *te-sik-kir*. For the character which I have marked ? (there being no instance given in *Br.* or *SAI.*) the variant, not only constantly in phrases throughout *AM.* but actually in duplicate texts (*AM.* 92, 4, 1, and Scheil, *RT.* xxiii, 1901, 134 ff., 4th paragraph), is IM.ŠU.RIN.NI = *tinuru* "oven", as might be guessed from the single character ("bread in an

9. [If from a man's eyes blood] has dropped and . . .

No. 36. *AM.* 16, 3 (K. 3320) + 12, 3 (K. 2575) + 13, 1 (K. 8110) + 18, 2 (K. 2545) + 19, 6 (K. 2533).

Col. i.

1. . . . these drugs . . . thou shalt put therein; to his eyes thou shalt apply; then . . . thou shalt put before his eyes; with rose-water thou shalt smear¹ his eyes . . .

4. An eye-application for the Hand of a Ghost: Sulphate of iron,² . . .

enclosure"). (See E. xiii, 8; xiv, 40.) Moreover, *AM.* 15, 6, 7, gives *ina ? te-ip-pi* "in an oven thou shalt bake" (and cf. a curious use 9, 4, 8). *Te-sik-kir* varies constantly in *AM.* with *BE-ir*, *BE* being *sikiru sa mé* (*SAL.* 872); E. (xiii, 8) showed that the variant *tesikir* might be connected with *sikrute* "als etwa gekocht" (cf. 78, 9, 6). Cf. *ina ? BE-ir GIBIŠ* (*DUL.DU*) "thou shalt roast in an oven, take out" (40, 1, 53; 68, 1 r. 4; 70, 5, 17; 76, 2, 3; 78, 9, 6, dup. of 81, 2, 12; 83, 1, 21) and particularly *ešteniš(niš) tabašal(šal) ina ? BE-ir GIBIŠ* "thou shalt boil together, roast in an oven, take out" (76, 2, 3), and "wash in water, roast in an oven . . . wash, *ina ? tatar BE-ir*, in the oven again roast" (42, 1, 5). The intention is to inspissate or condense the liquid, and it is thus possible that *sikru* gets the derived meaning "condensed", e.g. in *ina me kasi sikruti baħrute* "in rosewater, hot" (80, 1, 10, see *PRSM.* 1924, 3), *ina mé ŠE.NA.A sikruti tumašša'-šu* "thou shalt rub him with inspissated juice of vitex" (79, 1, 15). (Compare also *erā BE* = burnt (?) copper, No. 28, A, 26. The root is probably the same as *سقر* "scorched, heated" (Lane, *Dict.*, 1379).)

¹ *Tuħap[u]*, 𐎶𐎶𐎶 "rub".

² *TakMuza*, also occurring *PRSM.* 1924, No. 13, 6, 11. This stone is used about fifty times in *AM.* and is written *takmuzu*, *takmušu*, *takmuz(g)a*, *takmuši*; twice as "male" (7, 1, 10; 97, 4, 10); quantities, 1 *šu*, 30, 12, 5; 2 shekels (?), 62, 1, iv, 4; "fourteen *muzu*-stones," 47, 3, 9. In *AM.* it is almost always (if not always) used externally (cf. for the one possible instance of drinking, *AM.* 82, 4, 3); anoint, 29, 1, 5, 6; 33, 3, 6; 82, 4, 3; 89, 3, 3; 92, 4, 5; 94, 2, ii, 19; 96, 4, 7; anoint temples, 97, 4, 26; 102, 1, 16; 103, 22 (in oil on wool, 4, 6, 4; 20, 1, 15); for temples, 14, 4, 6; 102, 21; mouth, 78, 1, 29; eyes, apply, 14, 3, 8; 16, 3, 4; 19, 6, 12 (probably 12, 4, 4; 18, 9, 2); neck, 4, 6, 6; 7, 1, 10; ears, fumigate, 33, 1, 33; scorpion sting, anoint, 91, 1 r. 6; thread, put on neck, 47, 3, 9; *šimmatu*, 92, 5, 4; for ghost, anoint, 93, 1, 3, 5, 7; probably 94, 7, 7, 8; 96, 4, 9; 97, 4, 8, 10; 103, 7; for ghost, 16, 3, 14; 19, 1, 11; 76, 1, 2. Its meaning is indicated by *CT.* xiv, 14, K. 4396, 8:—

<i>takmu-zu</i>	<i>ša lib u-ru-la-ti-šu</i>	<i>pap-pal-tu ša bir-ki ameli</i>
<i>takHAR siparri</i>	<i>ameluti</i>	<i>takbir-ki ameli</i>

Cf. ib., 15, 31, 32, but separated from *takmušu*, ll. 19, 20; and particularly 14, S. 995, r. 2, *šer mu-u-[zu]*, as dup. of above. Note that these are texts containing explanations of mineral drugs.

Now there is no doubt that we have here a definite mineral *muzu* or *mušu*, but the phrase in the religious text *ZA.* iv, 254, 11, indicates another side, *māšu ša libbi urulati-šu iktib ilāni* "an issue from his foreskin is an abomination unto the gods". I agree rather with Jensen (*KB.* vi, 1, 374), who says it is probably "die stinkende Absonderung der Vorhaut", than Holma "the glans"; Ebeling (*ZDMG.* 1920, 187) is nearer, "Ausschlag (Ausfluss)." It is definitely a disease from *KAR.* 193, 12–15 (if a man's urine is like that of an ass, like yeast (dregs) of beer, of wine, *ŠE.TU* (= *šindu*, varnish, Thureau-Dangin, *RA.* 1920, 66, 29, or paint, *PRSM.* 1924, 25) *hi-li-ti* (from *hīlu* "gum"), i.e. "gummy varnish", that man is sick of *muša*). L. 16 (dup. *AM.* 58, 6, 2, as pointed out by E. xiii, 132) "if a man's penis *utakkasu* (pricks him, smart, *𐎶𐎶𐎶* 'sting, prick') when he micturates (or ?) ejects his semen, . . . his heart is 'caught', and he goes to a woman (and) is 'bound' (impotent ?), 'white blood'

-stone, white *mi'lu*-salt,¹ black *mi'lu*-salt, pearl,² tops (juice) of the male mandragora . . .

6. All these eleven stones and drugs thou shalt put in water, set under the stars, . . . put in oil, anoint his eyes, put in beer and he shall drink . . .

8. This in one month (and) twenty-one days . . . shall be healed.

9. If ditto, with "red stone", which is like opium,³ his eyes thou shalt anoint; If ditto, sulphate of iron, ditto.

10. If ditto, thou shalt bray ice (?) in curd, ditto; If ditto, thou shalt bray *lapis lazuli* from the mountains in curd, ditto.

(pus, gleet) continuously flowing from his penis, that man is sick of *muša*" (for his recovery *storax is to be introduced into the penis by a catheter, and he is to drink some *Solanum* in *mulu-tinna* beer, and a bandage containing pine-turpentine, fir-turpentine, and juice of *Nerium oleander* (?) in fat is to be bound on the end of his penis). The symptoms agree well with those given in Quain (*Dict. of Medicine*, i, 541) for gonorrhœa: "smarting in micturition" and subsequently a "copious yellowish-green discharge". In *mušû*, as Jensen saw, we have a definite medical equivalent for gonorrhœa (cf. *𐎢𐎱𐎲𐎠* as an issue of mouth or lips), an abomination to the gods, as in Lev. xv. Cf. also *AM.* 62, i, iii, 4, *lu mušu lu ku.gig*. It is therefore not improbable that we have a pun in the vocabulary quoted above: "mineral drug for issue from his foreskin, pollution (*pappaltu*, *𐎢𐎠𐎶𐎠𐎶𐎠*, Frank, *Stud.* i, 137; Holma, 97) of a man's penis: mineral *𐎢𐎠𐎶𐎠𐎶𐎠* (*𐎢𐎠𐎶𐎠𐎶𐎠* = *erû*, Schileico, *ZA.* 1914, 291) of bronze for (?) human beings = mineral for a man's penis." The scribe has attempted to derive *mucu* or *mušu*, the mineral, from the disease gonorrhœa (*mušû*, *𐎢𐎱𐎲𐎠*), for which I propose to show that the mineral is a cure.

Now the Greek *μίον*, with which *mušu* has great apparent similarity, according to Pliny, (*NH.* xxxiv, 31) sparkles like gold, when broken, and has the appearance of chalcitis, when tritured. In other words, he connected it with copper (i.e. the Assyrian "*𐎢𐎠𐎶𐎠𐎶𐎠* of bronze for human use"). Bostock (*Pliny*, vi, 198) quotes Brongniart that *μίον* is perhaps mixed sulphate of iron and copper; Berthelot (*Hist. des Sciences*, ii, 131) makes it sulphate of iron (more or less oxidized and basic, resulting from spontaneous decomposition of pyrites). Either sulphate of copper or iron will do as a remedy for the diseases quoted: the former for ulcers, as an injection for gonorrhœa, and as an astringent application to the eyes (*P.* 466), and the latter for amenorrhœa (internally), as a lotion for ulceration (externally), and as an injection for urethral and vaginal inflammations (*P.* 531). But whichever it be, *mušu* was certainly used for the same diseases as *μίον*, which is prescribed by Pliny (*ib.*) for diseases of the male generative organs, on wool for ulcers of the head, as an injection with oil of roses for ears, for granulation of the eyelids, for tonsils, etc. Clearly *mušu* = *μίον*, both as a word and as a remedy, and it is almost certain that *μίον* must have been borrowed by the Greeks from Assyria.

The quotation given above about the "issue from his foreskin" is no little evidence that the people who originally wrote this did not practise circumcision.

Note *CT.* xiv, 15, 19, 20, the male and female *mušu*-stone. Meissner (*Bab.-Ass.* i, 350) points out that there is a *Muši*-mountain mentioned by Shamshi-Adad, iii, 37, probably southwest from the Afshar Mountain.

¹ On the exact meaning of *mi'lu* see my *Chemistry*, 27.

² *Lulu*, *𐎢𐎠𐎶𐎠𐎶𐎠*. For pearls in eye-medicaments, see *SM.* ii, 101, 102. Cf. No. 44, 12.

³ Not *𐎢𐎠𐎶𐎠𐎶𐎠*, "cinnabar." At the same time cinnabar is used for eyes: *SM.* ii, 88, 98, etc. See *AH.* 46; opium is a hard, red-brown drug.

11. If ditto, carbonate of copper,¹ ditto ; If ditto, thou shalt bray kohl² in harlot's milk, anoint his eyes.

12. If ditto, thou shalt bray black iron-oxide³ in "mountain-oil" (petroleum), ditto.

13. Fir-turpentine, a little of some drug against pain,⁴ *storax, . . . roses, fat of reeds, magnetic iron ore,⁵ sulphate of iron, oil of . . . , old shell,⁶ wax, these eleven drugs as a mixture against the Hand of a Ghost thou shalt . . . , and apply to his eyes and he shall recover.

Col. ii.

1. . . . and cannot perceive, it is the Hand of Ishtar . . . , and in curd thou shalt bray, apply to his eyes and he shall recover.

3. . . . cannot sleep, out of all proportion(?)⁷ they (his eyes) are heavy . . . , in curd (and) mountain honey thou shalt mix (and) apply.

5. [If the . . . of a man]'s eyes is obscured(?),⁸ and the bed in the night(?)⁹ he cannot lift up,¹⁰ thou shalt roast juice (tops) of *Vitex agnus castus*, juice (tops) of figs, . . . , juice (tops) of nettles in water in an oven ; (then) pour it thereon : . . . cattle-dung together thou shalt pound (and) strain, mix with flour of roast corn, knead in rose-water, bind on : **Ricinus* he shall drink in beer, and he shall recover.

8. If a man [can see] nothing [by day], (but) can see everything by night, (it is called) "Sin-lurmâ".¹¹

9. If a man can [see] everything [by d]ay, (but) can see nothing by night, (it is called) "Sin-lurmâ".¹¹

¹ *Tak Mušgarru*, malachite. See my *Chemistry*, 94.

² GAB wrong ; read ²BI.ZI.DAM, i.e. ii R. 30, 31a, ²BI.ZI.DA = SU-U, and 33a, which must be ²BI.ZI.DA = guhlu.

³ *Tak KA.MI*. See my *Chemistry*, 122.

⁴ Cf. *AM.* 89, 4, 5.

⁵ *Tak KA.GIN.NA.DIB.BA*. See my *Chemistry*, 124, and cf. *SM.* ii, 707.

⁶ Cf. *AM.* 13, 3, 3.

⁷ *Eli minate-šina*.

⁸ *Šaddu*, perhaps *šad* "close up, obstruct".

⁹ Or "in his sight" (?).

¹⁰ Or does it mean "distinguish" ? By comparison with the succeeding text it refers to night-blindness.

¹¹ *Sin-lurmâ*, the name of the disease, just as others are called "Hand of Ishtar", etc. As it stands, there is no sense in *Sin-lurmâ* ("may the moon dwell (!)", or similar) ; a clue is furnished by l. 10, where obviously either *si-lu-ur-ma-a* (the verb denoting this particular form of eye-disease) is merely "*Sin-lurmâ*" formed into a quadrilateral, or "*Sin-lurmâ*" is a folk-etymology from *silurmâ*. The former is the more probable ; as a matter of comparison merely,

10. If a man's eyes suffer from "Sin-lurmâ"¹ (night-blindness), thou shalt thread *makut*² of the liver of an ass (and) flesh of its neck on a cord (and) put it on his neck, prepare a water-pot³; on the morrow thou shalt spread a cloth in the sun, prepare a censer of pine-gum: (then) thou shalt let this man stand behind the cloth in the sun. A priest shall take seven (rounds of) bread;⁴ he whose eyes are sick shall take seven (rounds of) bread: [(then) the priest] shall say [to] the sick man, "Receive, O clear of eye:" [the sick man shall say to the priest, "Receive, O dim⁵ of eye" (Col. iii, 1). . . . Thou shalt chop up⁶ the *makut* of the liver . . . , assemble some children and they shall say thus: ". . .", they shall say: thou shalt mix curd and the best(?) oil together, apply to his eyes.

4. [Ritual for] this: as before.

5. [Charm:] . . . receive: may Ea hear, may Ea receive . . . [Do not se]e, O clear of eye: see, O dim of eye. Recite the charm.

7. . . .⁷ and this charm . . . of the door(?) thou shalt put in his hand and he shall eat.

it is interesting to see how Sin could take over its form Si' in the West (see Johns, *Liber Censualis*, and my chapter in Woolley, *Carchemish*, ii, 135). At all events, we may sum it up that "*Sin-lurmâ*" means "night-blindness", or something like it, and that it was slurred into a quadriliteral *s-l-r-m*. (Cf. the similarity of remedies in Syriac and Assyrian in n. 1, p. 14.)

But out of this word arises the probability of the derivation of סִנְיָרִים, which has never been satisfactorily explained. Obviously it is not a Hebrew word: it occurs three times in the Old Testament, once at night ("so that they wearied themselves to find the door", Gen. xix, 11), and elsewhere (2 Kings vi, 18 bis), of temporary blindness. Its likeness to *Sin-lurmâ*, *silurmâ*, is most striking, particularly as Sin becomes סִן also in סִנְיָרִים. Note also W. Smith, *Dict. of the Bible*, ii, 418: "The idea expressed in Ps. cxxi, 6 ('The moon shall not smite thee by night') may have reference to the general or the particular evil effect; blindness is still attributed to the influence of the moon's rays on those who sleep under the open heaven, both by the Arabs (Carne's *Letters*, i, 88) and by Europeans." I was myself told by my Arab camel-man in Sinai that a headache which I happened to have one day was caused by my sleeping with my head unprotected from the moon.

¹ Si - lu - ur - ma - a : see preceding note.

² *Makut* : *makutu*, near *dilutum* "bucket" (*MA.* 540): מִכּוּת = "ship". But these are hardly likely as explanations; "strips" or "pieces" would suit the context, but even if it were *makkutu*, מִכּוּת would hardly provide a good philological comparison. The solution would agree with *SM.* ii, 663, but not with the ultimate procedure. *Gabidu*, for *kabidu*; cf. *SAI.* 6420, 6421, *HAR* = *kabidu*, *kabitu*.

³ *Agubbâ*.

⁴ Cf. Ebeling, *MDVG.* 1918 (ii), 33, l. 18 ff., 7 *ta-a-an* *GAR.MEŠ ina pitilti tašakkak(ak)*.

⁵ *Balša inī*, obviously in contrast to *namra inī*. Cf. *balša ina-ka*, *PSBA.* xxi, 41.

⁶ *Taḥarraṣ* (cf. *ḥirṣi*, r. 9). Cf. note 7.

⁷ . . . šu.si ḥa-še-e telikḫi. *HAR* = liver and *ḥašû*: šu.si is part of the liver (*Jastrow, PRSM.* 1914, 121). But this hardly agrees with the procedure of cutting it up.

9. . . . thou shalt [take away ?] the *makut* of the liver, and the pieces thou shalt . . . [and] thou shalt anoint his cheeks and [eyes] and he shall recover.¹

Col. iv.

1. . . . pine-turpentine, fir-turpentine, . . . -plant, . . . , *lolium*, a drug for pain, sulphur, *borax,² *asphalt,² . . . together thou shalt pound, therein antimony thou shalt put, and thy finger³ ? ?

5. . . . *Lolium*, hellebore,⁴ *maštabba*-plant, fir-turpentine, wax, *ammi, fat of *opopanax, seed of pine.

6. Eight drugs, a compound for eyes.

7. *Ammi, *Lolium*, roses, *asa foetida*, hellebore, *maštabba*-plant, tannin, fir-turpentine, mustard, on the fire thou shalt boil, in oil and wax of white honey apply.

9. Nine drugs, for mixing a salve.

10. ⁵ *Ammi, hellebore, roses, *maštabba*-plant, myrrh, seed of pine, shoemakers' tannin, seven drugs a compound for eyes, at the fire thou shalt roast, in fat, wax and curd thou shalt bray, apply to his eyes.

12. Black *mil'u*-salt, powdered arsenic,⁶ sulphate of iron, *Salicornia*-alkali, fir-turpentine, *storax, *Lolium*, tannin, sulphur, ox-fat, antimony, "needles" of antimony, šU.MULU⁷ . . .

14. Black *mil'u*-salt, sulphur, bitumen . . . , *Nigella*, roses, *Lolium* . . . ox-fat, marrow of "long" bone . . . a needle(?) . . .

No. 37. *AM.* 12, 4 (K. 4120) (*similar in part to* 18, 9 (K. 9503), *preceding* 12, 7, K. 10790).

1. If a man's eyes are troubled thou shalt bray white honey in curd (?) [and apply].

¹ For this treatment of night-blindness, cf. *SM.* ii, 97, for the same complaint, where the liver of a goat (or stag) is to be roasted, and when half-cooked the gravy is to be smeared on the eyes; and especially 663, where the liver of a horse is to be cut up, roasted, and then chopped fine and smeared on the eyes with oil of musk.

² See my article, *JRAS.* 1924, 454.

³ Cf. 77, 6, 7, and 101, 3, iii, 13.

⁴ See my article, *JRAS.* 1924, 669.

⁵ Cf. for this receipt *AM.* 8, 1, 17, and Scheil, *RA.* 1921, xviii, 1, p. 6.

⁶ Some form of the yellow sulphide; *PRSM.* 1924, 25.

⁷ See No. 28, A, 1, n. 1.

2. (Cf. 18, 9, 1 ff.) When his eyes perceive a dazzling(?),¹ it is the hand [of a ghost ?] . . . ; for his recovery, magnetic iron ore, mineral of lead, *mil'u*-salt, [black *mil'u*-salt ?], sulphate of iron, *ṣAB*-stone, lapis lazuli, *šubû*-mineral² *BAL*-mineral, male copper,³ . . . tamarisk-seed, laurel-seed, seed of male *Cyperus*, arsenic⁴: [these drugs together thou shalt pound (and) make] fine,⁵ in suet of the kidney of a black ox like tannin on copper thou shalt bray and [apply continuously to his eyes, and he shall recover].⁶

pine-turpentine(?) as a fumigation [thou shalt fumigate] his eyes and temples.

7. [When ditto ?], tamarisk-seed, laurel-seed, seed of [male] *Cyperus* . . .

9. [If the hand] of a ghost seizes him and before his eyes [it is] like a light . . . becomes like a goat(?), that man . . .

11. . . . pine-turpentine, fir-turpentine . . . thou shalt bray together . . .

No. 38. *AM.* 18, 9 (K. 9503, here for comparison).

2. . . . black [*mil'u*-salt], sulphate of iron, *ṣAB*-stone, cinnabar, . . . , green verditer, tamarisk-seed, laurel-seed . . . these . . . drugs together thou shalt pound (and) make fine, in suet of the kidney of a black ox [like tannin on copper thou shalt bray and] apply continuously [to] his [eye]s, and he shall recover.

6. . . . three times thus let him say: "Of Bêl and Beltis [the servant ?] am I" he shall say and shall recover.

8. Thou shalt take a . . . which stands(?) . . . roast it over the fire, bray (it) [in] honey (and) curd, apply to his eyes, and he shall recover.

No. 39. *AM.* 12, 6 (K. 3662).

(1-6. Various drugs, including *ur*(?)*zini*, turmeric, *eruca*, to be kneaded in cold water and bound on for fifteen days.)

¹ *Burša*; cf. *Enuma* NA ina *ênâvi-šu bir-ši* . . . , 85, 2, 4. Doubtful; hardly برشا scabies. *Biršu*, of stars rising (*MA.* 193), here perhaps the sudden dazzling of the eyes which sometimes temporarily obscures the sight.

² Vitriol, see my *Chemistry*, 110.

³ Cf. "male and female hæmatite" (Duval-Berthelot, *Hist. des Sciences*, ii, 163, quoting Bar-Bahlul) and *AM.* 7, 1, 10.

⁴ See No. 36, iv, 12.

⁵ *Tadalul* (cf. 18, 9, 4). Does this replace the usual *NAM* (cf. *NAM.TIG* = *dullulu*, *Br.* 2156)?

⁶ See Pliny, *NH.* xxxiv, 32, on chalcanthum, green vitriol or sulphate of the protoxide of iron, for eyes (Bostock), i.e. ferrous sulphate.

7. [If a man's] eyes are full of yellow rheum, thou shalt bray pomegranate-rind¹ [and apply].

8. If a man's eyes are full of yellow rheum, thou shalt bray pomegranate-skin [and apply].

No. 40. *AM.* 12, 9 (K. 13439, *probably part of* No. 26, K. 2573).

L. 6. "Incantation for failing eyes, for eyes . . ."

L. 7 ff. "Ritual for this: thou shalt take seven grains of *Andropogon-gum*(?) . . . in the night on the roof(?) before the star . . . In the morning before the sun riseth . . ."

No. 41. *AM.* 12, 11 (S. 1156, *now joined to* K. 2354, *CT.* xxiii).

No. 42. *AM.* 13, 2 (K. 2444). (*Obv. mutilated.*)

Rev.

1. Cantharides(?) . . .

2. Antimony in fresh(?) curd . . .

3. If a man's eyes a film² . . .

4. If a man's right eye a film² . . . , with a bistoury . . .³

6. If a man's left eye a film² . . . , with a bistoury . . .

8. If a man's eyes are sick . . . [thou shalt pound] the brain of an eagle in harlot's milk [and apply].⁴


10. Nettle-seed *sikti*⁵ . . .

11. If the pupils of a man's eyes a film(?) . . . thou shalt apply to his eyes. If ditto, gum of . . .

13. [If in] the eye of a man a film . . .

No. 43. *AM.* 13, 3 (K. 6974).

2. If a man's eyes . . . old shell of *Concha Veneris*(?)⁶ . . .

¹ Cf. *AM.* 9, 6, and Kū. iii, iv, 5. BAR = *ḫuliptu* (*SAI.* 1059) = ; either rind or bark (cf. my article *JRAS.* 1924, 454, where it is used of tamarisk). Pomegranate-rinds are included in a prescription in *SM.* ii, 93, when there is excessive rheum in the eyes. Note the difference in ll. 7, 8, which may be due to a perfunctory and slavish copying while collecting receipts from different sources. LA, *AH.* 279. I see that Ebeling, *Arch.* xiv, 1923, 28, had already suggested "pomegranate" as possible for *nurmû*, comparing Armenian. This suggestion must be taken, so far as it goes, to anticipate my *AH.* (1924), 175.

² *cuš.mi*, see *PRSM.* 1924, 28, n. 9.

³ Is this an operation for cataract or similar eye-trouble?

⁴ Cf. *SM.* ii, 706, a raven's brain rubbed on eyes, to see stars in the day-time.

⁵ See No. 33, 3.

⁶ LA *labira(ra) ša kibda* . . . (كبدۃ).

4. If a man's eyes bulge(?)¹ . . . the eye the dimness of the upper part(?)² . . .

6. If ditto, thou [shalt boil] *Lolium* in milk³ . . . fat of opopanax, hellebore, . . .

8. If ditto, corn-bread . . .

9. . . . *Lathyrus*-flour, fenugreek-flour, . . .

10. If ditto, *Ferula communis* . . .

No. 44. *AM.* 15, 6 (K. 1845) + *AM.* 13, 7 (K. 9247).

Col. i.

3. . . . in oil and copper-dust . . . in oil, copper-dust thou shalt bray, apply: honey . . .

5. . . . *Solanum*, green thou shalt press,⁴ its water in . . . in copper-dust and oil [thou shalt bray, apply].

7. Thou shalt bake . . . *kaz* in an oven, (until) there is not much (left) . . . alum, *storax, roses, in curd [thou shalt bray, apply].

9. . . . [thou shalt] reduce, bray, as an application thou shalt put it on . . .

10. . . . roses, roast fresh *Lolium*, in a cup thou shalt mix, [apply].

11. Thou shalt bray . . . roses in milk, [apply] to his eyes.

12. Thou shalt reduce black *mil'u*-salt, bray in curd, apply: If ditto, thou shalt bray a pearl⁵ in marrow of a sheep-bone, apply.

13. Thou shalt lay up a . . . -fish(?) in salt until sunrise, and (then) take it out, bray (it) in oil (and) copper-dust, apply.

¹ *Šuḥḥuta*. *SUR* = *ṣaḥatu* (Br. 2984): *karanu SUR*.(RA) (40, 4, 9; 50, 5, 3; 82, 2 r. 11) and *amēṣaḥit karani* (Br. 5011) are various forms in which it is used. "Press out" appears correct from 14, 3, 7, where a plant, still green, after being brayed, "its water *SUR-at*": cf. also 25, 6, 13. It is used of eyes, *ēne-šu uṣṣaḥata* (MA. 873).

² Does this refer to detachment of the retina, the first symptom of which is the loss of the field of vision, upper or lower (Quain, *Dict. of Medicine*, 1883, i, 487)? On *DUL-ma* see *PRSM.* 1924, 24, n. 5. It is a noun in 9, 1, 37, and 106, 2, 1; a verb in 8, 1, 22.

³ Cf. 8, 1, 20.

⁴ *Tuḥasa*. In *PRSM.* 1924, 12, n. 1, I thought that *tuḥasa* was the same as the Arab *حاس* "mix". But from a comparison with *AM.* 13, 6, 11, where the green plant is to be pounded, I am inclined to compare it to *سب* "press, squeeze", in spite of the sibilant.

⁵ See No. 36, 4.

14. . . . upon a bronze blade in curd thou shalt bray, apply.

Col. ii.

2. . . . gum of *galbanum . . .

3. If a man's eyes *š i š i tu*¹ . . .

4. If a man ditto, one shekel of cantharides(?) . . .

5. If a man ditto, one shekel of cantharides(?) in curd thou shalt bray, apply: fifteen grains . . .

6. ***Calendula* in curd [thou shalt bray, apply].

No. 45. *AM.* 14, 1 (K. 8349) (possibly the same tablet as *AM.* 18, 6, K. 8832).

1. . . . "long" bone . . . in equal parts thou shalt bray, in honey, curd, oil of cedar, copper-dust . . . [apply].

3. . . . with roast corn thou shalt bray, pour on his eyes.

4. . . . wax together thou shalt mix, in fat of "long" bone thou shalt bray, apply.

5. [If a man's eyes] . . . [and] he [cannot] distinguish . . . , that man's visitation(?)² is old and his eyes are failing, . . . thou shalt bray in curd, apply to his eyes.

¹ See No. 32, 5.

² *ki*, frequently in these texts with *mišitti*; the reading is shown 82, 2, 7. *Ana amela š i-pir mi-šit-ti šup - šu - ši u ri - mu - te* . . . *Sipru*, lit. "a sending," i.e. a happening, accident, visitation: "to heal a man of the visitation of a blow." With the present passage (in which it might perhaps equally well be translated "functions") cf. 90, i, iii, 16, *šumma ki-su iltabir*. At the same time I am not at all certain about this rendering.

Mišittu means "a stroke" (of paralysis) in *Bab. Chron.* iii, 20, where Menanu, the king of Elam, *mišittum imišidsu-ma*, his mouth is stopped and he cannot speak, and he dies within the year. But 79, 1, 11, *šumma NA mišitti kabli gig atallukam la idi* "If a man is hurt by a blow on the loins, (so that) he cannot walk," followed by elaborate poulticing and massage, appears to be much less serious than paralysis of the lower limbs. The following are examples: *šumma NA mišitti pani išu ši-šu i* . . . "If a man has a blow on the face, his face . . ." (76, 5, 11); [*šumma amelu* (?)] *mišitti pani mašid-ma talamma-šu išammam-šu* "[If a man (?)] has been struck a blow on the face and its surrounding (flesh) poisons him" (77, 1, 1, *talammu* from *למה*, like *tabannu* from *בנה*); (ib. l. 2) . . . *mišittu imšid-su-ma lu imitti lu šumeli PA-iš* . . . "a stroke has struck him and either right or left is stricken (?)" . . . ; *šumma NA mišitti kišadi gig* "if a man is hurt by a blow on the neck" (79, 1, 9); similarly on the foot (l. 24), or on the side (*aši*, l. 21); *šumma NA mišitti TE iši(ši)* (79, 1, 6), or *gig* (76, 5, 9), or *INIM.INIM.MA šumma NA mišitti TE iši* (76, 5, 4). *šumma NA mišitti amiti gig* (79, 1, 17, cf. 77, 1, 7, 9) looks rather like a ghostly attack than paralysis like death. In some cases the verb appears to be absent: *šumma NA mišittum - ma kat-su u šepi-šu* . . . (82, 2 r. 8, cf. obv. 4, *mišittu-ma*; also l. 1); *UL mišitti murus-su* (50, 4, 7, cf. 6).

7. . . . pine-turpentine, fir-turpentine, flour of roast corn thou shalt pound, sift, mix in beer, bind on his eyes.

8. . . . an application¹ to the eyes.

No. 46. *AM.* 14, 3 (K. 5415 A), probably same tablet as *AM.* 14, 2 (K. 11723).

2. . . . mercury, *liquidambar . . .

3. . . . pine-turpentine, fir-turpentine, kelp(?), *asa* (*dulcis*) thou shalt bray, in a copper [pan(?) thou shalt mix] . . .

4. . . . mustard, ***Calendula*, *corn-marigold, *tarhu* on his neck [thou shalt put] . . .

5. . . . ŠAB-stone thou shalt bray, put in oil, anoint the middle of his eyes . . .

6. . . . thou shalt apply, with tamarisk-water for twenty days thou shalt wash his eyes, and the tamarisk-water three times thou shalt pour away, and he shall recover.

7. . . . green thou shalt bray, its waters thou shalt press, leave it under the stars, ditto.²

8. . . . sulphate of iron, tamarisk-water which has been set on the fire and . . . has been taken out therefrom, fat of a gazelle's bones together thou shalt bray, apply . . .

10. (Cf. *KAR.* 205, 4.) . . . cattle-dung, mustard, hellebore in wool thou shalt roll, put on his neck [and he shall recover].

11. [If] either (a demon of) evil intent, or . . . , or anything evil³ . . . seize him, for his recovery [thou shalt do this].

13. Thou shalt take . . . , on a thread of white wool thou shalt thread it: laurel(?)-root, . . . garlic, *asa* (*dulcis*), sulphur, alkali, these seven drugs

KI occurs as follows with *mišittu*: *šumma KI mišittu ša pi-šu* DIB . . . "if the accident of a blow on his mouth has fallen upon him" (78, 1, 5); [*šumma*] *KI mišittu ša miḥri* TAK "If the accident of a blow on the *miḥri* (Holma, 158) has happened" (77, 5, 17, cf. 16: 76, 2, 8, GAB.RI-tum); *šumma KI mišittu ša arki* TAK (a blow on the back) (77, 1, 11); [*šumma amelu* (?) *mišittu pani mašid-ma talamma-šu išammam-šu* KI [*ka* (?)]-*bar-ti* ["If a man (?) has been struck a blow on the face and its surrounding (flesh) poisons him, it is the accident of a swelling (?)"] (77, 1, 1); INIM.INIM.MA KI *mi-šit-tu* . . . (60, 3, 8) followed by *šumma KI NA maš-di ša* GAB.RI . . . zu (l. 9) without *mišittu*; *šumma ana KI kat edimmi la-az* . . . "If for the visitation of the hand of a ghost . . . (95, 1, 4); cf. 99, 3 r. 11, *Ana KI kat edimmi la-az-zi*.

¹ *Tipu*, cf. *AM.* 16, 1, 10, *annu ti[pu ša ēnā^{II}]*, perhaps 9, *te-pu*; *KAR.* 191, iii, 10, of drugs as *ti-pu ša KU.GIG*; *AM.* 15, 6, 9, *kima tiḫi te-ti-ip-[pi]*, 126. Pa. *imposuit* (*medicamentum*) as in *PRSM.* 1924, 27, n. 1.

² Cf. 25, 6, ii, 13.

³ *KAR.* 184 rev. 2.

. . . thou shalt fold wool: as [thou foldest] the folds, thou shalt recite [the charm] "May . . . give thee rest", the neck . . .

No. 47. *AM.* 14, 2 (K. 11723, *see preceding*).

4. [Incantation against] (a demon of) evil intent . . .

5. . . . on a thread of red wool thou shalt thread; the drug . . . , *Crataegus azarolus* (?), *kanšam*-plant, tamarisk-seed . . . on his forehead thou shalt bind . . .

(See also *AM.* 48, 7, and 76, 1.)¹

No. 48. *AM.* 16, 1 (K. 2500 + 7933) (*follows AM.* 12, 1, *in the same series*). *Obverse.*

1. [If a man's eyes] are full of . . . , thou shalt mix *Lolium* (and) flour of parched corn in beer and bind on: for three days to his eyes [thou shalt do this], renewing² (it) thrice daily; on the fourth day thou shalt surround³ his eyes with *suadu* (and) opium, water in . . . ; . . . (?) . . . (?) of clay⁴ and once, twice, or thrice his eyes thou shalt press: marrow of gazelle-bone to his eye[s thou shalt apply]. Then in opium thou shalt bray antimony (and) apply it to his eyes; thou shalt bray *gall-apples (and) apply dry to his eyes.⁵ Thrice daily thou shalt renew (it); thou shalt mix a paste⁶ of *mazi* (?), *barḫuš* (v. tamarisk), seed of *ḫutru*, . . . , parched corn, *Lolium*; apply it dry to his head, bind his head, and for [three] days [do not take off]. On the fourth day thou shalt take it off and shave his head: apply thy paste to his eyes, [and he shall recover].

8. *Storax, cantharides (?), "salt of Akkad," alum, *Salicornia*-alkali, myrrh, sediment of the river (?),⁷ roses, total eight drugs as an application for when the man's eyes are scorched by the sunlight⁸ and . . .

10.⁹ *Storax, alum, "salt of Akkad"; this is an appli[cation for the eyes].

11.¹⁰ Fir-turpentine, flour of roast corn, roses; this is an [application for the eyes].

¹ Note that *AM.* 14, 7, is the tablet next following Kū. iii, and may be part of the same tablet as *AM.* 99, 3; 15, 3, has been joined to 73, 1; 15, 2, has been joined to K. 2574 (*CT.* xxiii, 39 ff.).

² ŠAR = *uddušu*, *SAI.* 2840. Cf. *PRSM.* 1924, 4, n. 3.

³ *Takaddad*: *kadādu* and *kamū* are both translations of ŠAR (Br. 1758, 1759).

⁴ Cf. *SM.* ii, 70, "if it be necessary to treat the whole head, we smear it over with clay mixed with vinegar."

⁵ Cf. 92, 8, 9.

⁶ *Ulap*; see *JRAS.* 1924, 453. *Mazi*, doubtful.

⁷ See No. 62, n. 1.

⁸ See *AM.* 20, 2, 7; 39, 1, 41; 41, 3, 7, 9.

⁹ Dup. *KAR.* 183, 9.

¹⁰ Dup. *KAR.* 183, 7.

12. [If a man's eyes have a dazzling(?),¹ he shall go to another house, and the door being shut as if . . . the dazzling(?), ditto, "Away with your dazzling(?)" [he shall say].

14. [If ditto], he shall go to [a house] of darkness² and the door being shut as if . . . the dazzling(?) ditto, "Away with your dazzling(?)" [he shall say].

15. [If there be on a man's eyes a film,³ fir-turpentine, pine-turpentine, gum of **Pinus Halepensis*, seed of . . .

17. [If within a man's eyes hair sprouts and his eyes hurt, salt, tannin (v. . . .), fat of . . . alum, in equal parts thou shalt bray, mix in curd, apply to his eyes . . .⁴

19. [If a man's [eyes] are full of flesh growing⁵ . . . nettle-[see]d in honey thou shalt bray, apply:

If [ditto] . . . arsenic⁶ in curd thou shalt bray, apply: If [ditto] . . .

22. [If a man's [eyes] are full of flesh growing and matter(?)⁷ comes, for his recovery . . . *opopanax, *storax, cantharides(?), salt . . . [in blood] of cedar or in oil of cedar thou shalt mix, apply . . .

25. [If a man's eyes are full of flesh and blood, . . . cantharides(?), *Lolium*, . . . drugs . . .

27. [If a man's [eye]s are full of *guḱani*⁸ . . . seven days on the threshold(?) . . .

No. 49. *AM.* 17, 1 (K. 6560) + No. 8, *AM.* 3, 5 (*PRSM.* 1924, 13) (possibly belonging to K. 7953, *AM.* 64, 1).

I, 2. (For itch, probably) . . . with *uṣ.gul*⁹ thou shalt anoint: the

¹ *G(k.k)iddag(k.k)ida.*

² A tomb?

³ *Libištum*, lit. "a covering, tunic."

⁴ Cf. *SM.* ii, 102, "Now as concerning the superfluous hairs which grow inside the eyelids and pierce the eyes."

⁵ Cf. the use of *ḫḫ* in *Jer.* xii, 2; *Ho.* xiv, 3. For the disease cf. *SM.* ii, 659, "For the eyes which have flesh in them."

⁶ See No. 36, iv, 12.

⁷ *u* (?) (= *damu*: *sarum*, Br. 8739; cf. the *u* in *U.BU.BU.UL* = probably *bubultu* "ulcer" (see *Kū.* iii, i, 8; *Holma.* 150; *E.* xiii, 132). Cf. *AM.* 20, 2, 5, 7.

⁸ *Guḱani*, cf. *CT.* xxiii, 23, 2; my translation, *AJSL.* 1907, xxiv, 338; Jastrow, duplicate, *Trans. Coll. Phys. Phil.*, 1913, 375; Daiches, *ZA.* 1912, 382. *Nḫḫ* is a worm, but although *SM.* ii, 665, prescribes for worms in ears, there is nothing similar for eyes. It cannot be *gūglā* of *SM.* ii, 100?

⁹ Cf. 5, 5, 2.

skin of an ass in fire thou shalt reduce, bray, apply¹: hay in fire thou shalt reduce, apply to the affected surface¹ with *ta'a* (fat?) of a male sheep anoint the affected surface: leather thou shalt dry, pound,² [apply]: . . . "ox of the river"³ in fire thou shalt reduce, apply to the affected surface: ***Calendula* thou shalt bray, anoint the affected surface: . . . thou shalt rub, thou shalt cover(?)⁴ the affected surface with a gold ring.

II, 1. If a man is full of itch,⁵ fennel (and) . . . [toge]ther thou shalt bray, mix in oil, [anoint and he shall recover].

2. If ditto, **Ricinus*, sumach, thou shalt bray, in . . . wash, the rind of . . .

3. If ditto with oil of fishes' inside(?)⁶ thou shalt anoint . . .

4. If ditto, "scab of the housewall" (= calcium nitrate?)⁷ thou shalt rub, and anoint(?) . . .

5. **Storax*, fennel, **Ricinus*, these three drugs for itch . . . , root of *barhuš*, root of tamarisk, cummin . . . [thou shalt apply].

No. 50. *AM.* 17, 4 (K. 5906).

3. Marrow of a male sheep's "long bone" . . . , *Nigella*, pomegranate-water . . . thou shalt mix together, in honey, curd, cedar-oil . . . [thou shalt apply].

6. ⁸ If a man's eyes do not see, that man [has walked(?) in] the heat of the day; $\frac{1}{2}$ shekel of **storax*, $\frac{1}{4}$ shekel of "salt of Akkad" [in honey(?)] (and curd) . . . [thou shalt bray, apply].

8. If the object of vision of a man's eyes is multiplied,⁹ fat of a black snake¹⁰ . . . , fat of a lion,¹¹ *asa foetida*-gum, opium (*v.* gum of **Pinus Halepensis*), *Salicornia*-alkali . . . in equal parts in copper-dust in mountain-honey thou shalt mix, bray, apply . . . to his eyes apply and his . . .

¹ i.e. as ashes.

² Cf. *SM.* ii, 657, old soles of sandals for sores in head, and particularly *PRSM.* 1924, 15, No. 15, 2.

³ Not "hippopotamus" here (*MA.* 48).

⁴ *Ta-kas*, possibly connected with כוס "cup", but uncertain. *Anšabtu*, a finger-ring (Holma, *WB.* 5). Cf. *AM.* 65, 5, 24.

⁵ *Guraštu*, *PRSM.* 1924, 10, n. 1.

⁶ Cf. the "garum" of Pliny (*NH.* xxxi, 43) prepared from the intestines of fish, from which "garum" came the refuse called "alex" (ch. 44) used for scab in sheep and ulcerations.

⁷ *PRSM.* 1924, 4.

⁸ Probably duplicate *AM.* 18, 4, whence the restorations.

⁹ *Diḡil éná* ¹¹. *šu mádi*, cf. Kü. ii, iii, 49, "If a man drinks beer and *išdir*. *šu palḡa diḡla mádi*."

¹⁰ Cf. *AH.* 252, l. 14, [šér] *širi ḡalmi* = the *ḡadanu*-plant.

¹¹ = opium, *AH.* 5, l. 69.

No. 51. *AM.* 17, 6 (K. 11568) + 18, 8 (K. 13500).

Col. i.

1. . . . dates, 2 shekels of gum of *galbanum(?) . . . [scab ?] of the wall¹ together in oil thou shalt mix (and) bind on.

3. . . . their sight(?) . . . For their recovery fir-turpentine . . . , . . . , cantharides(?), these four drugs in equal parts [thou shalt mix, bray, in oil] of cedar anoint, apply to the affected surface, bind on, and he shall recover.

Col. ii.

1. . . . (it is) the "Crushing of Ishtar"² . . . on the affected surface thou shalt anoint curd, [and he shall recover].

3. For the "Crushing of Ishtar" . . .

4. For the *erimu*³-skin-trouble . . . these three drugs together thou shalt bray . . .

No. 52. *AM.* 17, 5 (K. 3642).

1. To remove soreness⁴ anoint thereon with the urine of a white dog, [and he shall recover].

2. For ditto, an egg from a nest which has been spilt on the ground [thou shalt anoint(?)] thereon.

3. For ditto, thou shalt bray mustard, *asa foetida*, hellebore, . . . , *ammi, *mint, lupins, [**Calendula* ?], *corn-marigold, male mandrake-root, licorice-root, . . . , **Anacyclus*, in scented(?)⁵ oil without a meal [let him apply ?].

7. For ditto, thou shalt bray *asa foetida*-root, in beer without a [meal let him drink ?].

¹ See No. 49, ii, 4.

² Cf. *AM.* 44, 1, ii, 10.

³ *Erimu*, a skin disease (Dennefeld, *Geburts.*, 306 r. 17). Cf. the plant "*erimu* (probably *šam erimu* "plant for *erimu*", *AH.* 58). Cf. 𐎶𐎵𐎶𐎵 "a rough place", i.e. hence roughened or chapped skin. *RA.* 1913, 77 gives *DAR.A* = *e-ri-mu*.

⁴ *Umšatu*. Cf. *AM.* 18, 3, 1, "If he have *umšatu*," **Ricinus*, alkali, etc., being applied locally. Here *Ana umšati nasaḫi(hi)* "to remove *umšatu*" (apply the urine of a white dog, or various other remedies; cf. l. 10). *Umšatu* may occur *ina lib uš-šu* (in the middle of his penis, 22, 1, 19). In 40, 5, 5, after anointing, *umšate uk-ta* . . . It is therefore an ailment, probably a skin-trouble. Holma (p. 34) quotes S. 1419, 6, *šumma umšatu* (DUB, "Aussatz, o. ä.") *elanu u-ru-uḫ* (hair) *imni šaknat*; (p. 96), K. 4020, *šumma birku rabi-ma, arik-ma, ina libbi* or *ina pi birki-šu umšatum*; (p. 162, n. 4), *SAI.* 2597, DUB = *umšatu*, quoting Meissner, *Supp.* 10a, K. 4020, "Speziell Geschlechtskrankheit." I doubt this, and prefer to see in it 𐎶𐎶𐎶𐎶 "raw flesh", i.e. sore skin (Holma, KB. 5; Meissner, *Bab.-Ass.* ii, 291, "Geschwür").

The drugs certainly coincide with the expected treatment.

⁵ *DAR.GA*, Kū. 110.

8. For ditto, *Salicornia*-alkali, myrrh, . . . pomegranate-rind, roses, together thou shalt bray [and apply] . . . destroying (?) soreness, *Salicornia*-alkali . . .

No. 53. *AM.* 18, 1 (K. 13465).

A mutilated eye-text with similarity to *AM.* 9, 1, 22 (cf. l. 7, A.GA), and 25.

No. 54. *AM.* 18, 3 (K. 10535).

1. [If a man] have soreness, **Ricinus*, *Salicornia*-alkali, . . . fennel, in oil of *storax thou shalt bray, in . . . in mountain-oil thou shalt anoint him and [he shall recover].

4. [If ditto], myrrh, pine-turpentine, thou shalt bray, in [. . . -oil thou shalt mix] . . . for fourteen days thou shalt bind on [and he shall recover].

6. [If a man's] right eye is inflamed (swollen) and te[ars flow] . . . for his recovery . . .

No. 55. *AM.* 18, 4 (K. 9555). (Ll. 6 ff. are probably duplicate of *AM.* 17, 4, 6.)¹

No. 56. *AM.* 18, 6 (K. 8832). (Possibly same tablet as *AM.* 14, 1, K. 8349.)

3. . . . thou shalt mix, rub.²

4. [If a man's eyes are sick³], tears flowing, the eyes being full of film . . . *storax, cantharides (?) . . . [in oil of] cedar thou shalt mix, apply to his eyes and he shall recover.

7. [If a man's eyes are sick] . . . the object of his vision⁴ being indistinct (heavy), to remove the white(?) which is on the pupil⁵ of his eyes . . . [in] oil of cedar thou shalt mix, apply to his eyes and he shall recover.

9-10. Mutilated, but similar.

No. 57. *AM.* 18, 7 (K. 9869).

5. . . . Alkali, savin (?) (or tragacanth(?)),⁶ ***Conium maculatum* . . . , the plant "raven's-foot"⁷ . . . , wherein *katiki* (?)⁸ comes forth, thou shalt pound (and) strain . . .⁹ either in *mulu-tinna* beer [or in . . . thou

¹ 18, 5, joins 73, 1.

² *Tetenik[i]*, *PRSM.* 1924, 4, n. 6, and see Ebeling, *Arch. f. Gesch.*, xiv, 1923, 35.

³ Cf. 9, 1, 31.

⁴ *Di-gal*, from l. 9, cf. *di-kal*, 9, 1, 32, and *di-gi-il*, 17, 4, 8.

⁵ Cf. *PRSM.* 1924, 28, n. 10.

⁶ See *JRAS.* 1924, 452, n. 7.

⁷ *AH.* 255.

⁸ Text re-examined. *Ka* might be *Kur dis*.

⁹ . . . *iš du* 'i, meaning doubtful.

shalt knead] . . . for one hundred days he shall drink . . . [(these) prescriptions ?] have no equal . . .

(L. 11 indicates an eye-text.)

No. 58. *AM.* 18, 10 (K. 4116).

1. . . . urine . . . the middle of his eyes . . .

4. When a man's eyes . . . , a drug against pain . . .

6. To appease . . .

7. Fat, shell, salt, to the middle of his eyes [thou shalt apply] . . .

8. Thou shalt bray salt besides (?) **Ricinus* in honey [apply] . . .

9. If a man's eyes . . .¹

No. 59. *AM.* 75, 2 (K. 6629). A fragment of medical prognostics.

Ll. 5-8, *pa'sat*, *pa'sa*, of eyes, may be either פַּי "flow" (i.e. stream with water), or *pāšu* "bruise", less likely. *Pa'zutam* is applied to roses (see No. 28, A, l. 24), which, with ground *Lolium*, are to be made into a *rabiku* and eaten in oil and honey. Ll. 9-11, either eye or both may set up (*nadû*) IM.MAL.LI = *kalû*. *Kalû* is a difficult word: IM.GUŠKIN ("gold clay, gold earth") = *illur panî* ("face bloom")² = *kalû* (*SAI.* 6352), and on *CT.* xix, 21, 32, it is followed by IM.DIR (= "red clay," *šeršerru* "red ochre"). "Face bloom" may be rather the lighter tint of the Arab than the ruddiness of the Northern European (probably represented by *kalgukku* "red *kalû*", *MA.* 383). *Kalû* must be an earth of a golden-brown colour (paralleled by IM.UD "plaster, gesso", IM.DIR "red ochre"), probably ὤχρα "yellow ochre", the reference in this eye-text being to the muddy-yellow appearance of eyes in jaundice.

Ll. 12-16, *tarkat*, *tarka*, of eyes, in ll. 15, 16, followed by "and will not open". *Tarāku* appears from *MA.* 1193 to mean "to beat" and "to fail" (ترك "abandon", תרץ "destroy"), probably here with the intransitive sense.

¹ *AM.* 19, 1, and 20, 1, dup. of K. 2574, *CT.* xxiii, 39 ff.

² *Illuru*, long known as equivalent for "flower" (*MA.* 49; *HWB.* 76). *I. sámu* = "scarlet anemone" (*AH.* 56), so that *i.* must be the calix or bowl-like form of the anemone (rose, poppy). King, *CT.* xxvi, 24, 32 ff., translates the description of the "female colossi of alabaster and ivory" *ša illuru našû kitmusa rittašin* "wearing horned-headresses (?) having bent talons", but I think it should be "which bear up the *calix*, their forelegs bent". The "calix" is the great column-base carved in form of a flower, borne on the backs of colossi (e.g. the picture of the model of a female colossus standing, bearing such a base, G. Smith, *Ass. Disc.* 174; for such a calix (without a beast), Perrot, *Histoire*, ii, 223, and Woolley, *Carchemish*, ii, 155; for a couching beast with bent forelegs bearing a column, Pottier, *Ant. Assyr.* 144; Ménant, *Glyptique*, ii, pl. 10, 4). *Illuru* thus certainly means "calix", especially (with *sámu*) of the red anemone; hence *pāri Ašur-lî* . . . *illuriš usimu* (*Sarg. Cyl.* 33), paralleled by *mašak A. akus* ("the skin of A. I flayed", Khors. 56), must mean that Sargon tricked it out like a flower-calix, or (red) anemone, probably dyeing it red like the skin of Ilubidi (*Cyl.* 25). *Illur panî* would thus parallel our poetical "bloom", "roses", "damask", of cheeks.

No. 60. *AM.* 94, 8 (K. 7279), *similar*.

For *hupti éná*¹ see No. 28, A, l. 36. *Šadira*, probably 𐎶𐎵𐎶𐎵 "be afflicted with nausea", in Etpa. "be disturbed".

No. 61. *AM.* 105, 2 (K. 3957), *similar*.

Ll. 8, 10, *iššanunda*, of the eyes, from *šādu*, lit. "hunt". *Iššanunda* is used of demons who press on the land like a storm (*abubu*) (*Devils*, i, 63, 11); of eyes, 13, 4, 1 (*NIGIN-du*); 22, 2, 1 (*NIGIN.MEŠ-du*), cf. 35, 7, 2; 85, 1, vi, 5 (*iš-ša-nun-du*); 14, 5, 9 (*i-ša-nun-du*, perhaps not eyes); uncertain, 14, 5, 12 (*i-ša-nu-du*); 97, 4, 6 (*iš-ša-nun-du*). In a prayer to the Sun-god (97, 1, 19) the suppliant says ŠAK.KI^{pl}-MU *i-ḫi-is-su-u* IGI ^{pl}-MU *NIGIN-d[u]*, so that it is probably "oppress" in the sense of "ache", rather than "hunt" = "roam" = "roll".

No. 62. *AM.* 92, 8 (K. 2508).

1. . . . into his eyes thou shalt blow . . . ditto.

3. . . . thereon shell, fine oil . . . thou shalt burn, the smoke of the . . . (?) . . .¹ to his eyes thou shalt apply, and he shall recover.

¹ IM.TIG.EN(?) .NA. IM.TIG occurs in *AM.* alone (3), 31, 7, ii, 10; 51, 1, 12, glossed IM.TIG.EN.NA; 78, 7, 7; in IM.TIG.EN.NA (13); 7, 3, 2; 45, 6, 11 (IM.TIG.EN); 48, 1, 3, 6; 48, 3, 3; 51, 1, 12; 54, 1 r. 11; 58, 2, 3; 75, 1, 33; 78, 5, 9; 78, 7, 3, 6; 79, 1, 14; in IM.TIG.GAR.RIN.NA (6) 5, 5, 11; 23, 8, 4; 40, 5, 11; 43, 2, 7, 9; 44, 1, ii, 6. (Uncertain are 7, 4, ii, 4; 16, 1, 8; 29, 5, 4; 51, 1, 6; 53, 1, iii, 5; 82, 1 r. 4.)

IM.TIG = *kadutu* = *didu* (i.e. *fitu* "mud"); IM.TIG.EN.NA = *kadut* (and *kadû*) *šikani* or *šiknu sa nâri* "bed of the river". For these see Del., *HWB.* 581, and for a short discussion on the medicinal use of this "bed of the river" see Kû. 102. It also = *ḫa-a-pu* (Smith, *CT.* xxxvi, iii, 11; *AH.* 257). IM.TIG.TIN.NA = *kadutum šikari* = *šuršummu ša bi.šag* ("lees, yeast of *kurunnu*-beer"); IM.TIG.A.AB.BA = *kadut tâmti* ("of the sea"). IM.TIG.ID.DA = *kadut nâri* ("of the river"). See *HWB.*, ib., and Br. 8406, 8407. There is little doubt that the accepted translation of Kûchler is on the right track, but it is difficult to settle the exact medical use.

In medicine IM.TIG.EN.NA is usually drunk for stomachic troubles (45, 6, 11; particularly 48, 1, 6, brayed and drunk alone in beer); chest (51, 1, 12), anus trouble (58, 2, 3). But it is also used externally, $\frac{1}{2}$ *ḫa* in poultice for stomach and back (Kû. ii, 1, 4), a very small amount. I had thought of sulphate of magnesia (Epsom salts) as a possibility, but the curious external use is a little against this, and also we should have expected it to have been defined by the word "salt". At the same time hydrated magnesium sulphate is found "in solution in sea-water and in mineral waters; also as efflorescent crusts and masses, as in the limestone caves of Kentucky and encrusting serpentine and other rocks rich in magnesium" (Rutley, *Elements of Mineralogy*, 166). The Admiralty Staff, *Geology of Mesop.*, 14-15, gives the bulk of the dissolved salts in the sediment of flood water as bicarbonates of lime and magnesia and some potash. The Assyrian doctors may have used this sediment internally on this account. There is some similarity to Pliny's "flower of salt" (*NH.* xxxi, 42), found in Egypt, brought down by the waters of the Nile, which is sophisticated and coloured with red earth, the sediment being even shaken to renovate its saffron colour. When drunk with wine and water it has a purgative effect, and it is used in detersive compositions, and for removing hairs from the eyelids. IM.TIG.GAR.RIN.NA is used externally (apply, bind on, for itch, etc.). GAR.RIN.NA is unknown, and hence it is difficult to identify the drug.

6. [If a man's] [eyes] . . . and is heavy, for ¹ his recovery *asa foetida*-gum . . . eighteen months(?) . . .(?) ²

8. . . . five grains of shell of *storax(-fruit) in oil thou shalt bray, apply.

9. . . . thou shalt apply dry.³

C. VARIOUS DISEASES OF THE HEAD, &C.

No. 63. *AM.* 21, 2 (K. 6196), which follows *AM.* 1, 1. Cf. 22, 2 (K. 3550); 43, 5, 7 (K. 9441); 54, 3 (K. 8716); 56, 1 (K. 8248); *CT.* xxiii, 46, 26; *VAT.* 8968, 1 (E. xiii, 4).

1. If a man's head hurts him, his tongue pricks him, his eyes [trouble ⁴ him], his [ears] sing, his throat chokes him,⁵ his neck-muscles hurt him, [his] breast, [his shoulders and his loins] ⁶ hurt him, his groin ⁷ . . . his

¹ Re-examined: *ana* should be inserted in my copy.

² *ZI HA TI*: hardly *innasiha(ha) ibaluš* "it shall be removed, he shall recover".

³ Here should be added a note on *AM.* 76, 6 (K. 3719), obviously connected with *AM.* 4, 1 (K. 2416), *PRSM.* 1924, 12. L. 9, "[Incantation] to turn grey hair black." L. 10, "thou shalt take the head of a male *išsur hurri*, boil, . . . apply, and the grey hair shall turn black." (Cf. *PRSM.* ib., 16.) I prefer the old idea of Houghton (*PSBA.* viii, 107) for *išsur hurri* "bird of the ravines" (better "cave-bird", which Langdon, I see, maintains in his *Babylonian Wisdom*, 59) to Delitzsch (*Ass. Studien*, 113) "hawk". The latter depends on حُر "hawk", and the Assyrian synonym for *išsur hurri*, *busu* (as it has been read) بَاز "hawk".

But I think *hurri* is more probably here the ordinary word "cave", חֹר. Moreover, I doubt the reading *bu-su* without a long vowel in either syllable; it is far more probably *sir-su*, and we may identify *sirsu* with שִׁרְסָן, comparing Lev. xi, 19, 20: וְאֵתֵּי עֲטָלָהּ: בָּל . . . שִׁרְסָן הָעוֹף הַלֵּךְ עַל־אֲרְבַּע " . . . and the bat. All fowls that creep, going upon all four", a description of the bat, to which anyone who has seen a bat shuffling along the floor of an Eastern khan will testify. Cf. *birká ša uktassá sir-si-[iš]*, the comparison being to knees bound "like a *sirsu*" (*VR.* 47, b 25, where *sir-si* = *iš-sur hur-ri*). The simile must be from the bat where the legs are included in and joined by the wing-membrane.

Some evidence may be drawn from the fact that the equation *sirsu* = *išsur hurri* (*CT.* xiv, 4, 1, 7) is immediately followed (l. 8) by *du-u-du* = *ip-pil-tum*, although I admit that just a position in syllabaries carries little weight. But *ddu* must be עֲטָלָה "bat", and *ippiltum* (which I prefer to Delitzsch, ib. 114, *ib-ne-tum*, אֲבִנִיתָא) will then be the uncouth עֲטָלָה, by some metathesis due to *l* in the word.

For comparative purposes I add K. 5418, i, 5 (quoted Del., *HWB.* 292), *šabē pagri išsur hurri* "men with bodies of *išsur hurri*", where "bats" is at least as probable as "hawks", and D.T. 59, 11 (ib.), "like an *išsur hurri* ina narbašiki (in thy dwelling)." *SM.* ii, 690, prescribes the head of a bat boiled in oil, for making hair grow; on the other hand, p. 702 recommends a hawk's blood. (For bats in caves see Layard, *Nineveh and Babylon*, 307.)

⁴ [*Išsanundu*], see No. 61, ll. 8-10.

⁵ *AM.* 22, 2, 2, *iš-hat-su*, the usual word for pressing grapes. See p. 45, n. 1.

⁶ *Naqlabu*, Holma 57, *Weiche* (?).

⁷ *Sapulu*.

hands hold poison, his fingers . . . cramp¹ him, his stomach is inflamed,² his bowels are hot,³ his knees . . . him, his flesh holds poison . . . [instead of ?] speaking . . . (?)⁴ . . . with his stomach he speaks . . . , is delirious⁵ . . . (*remainder broken*).

No. 64. *AM.* 22, 2 (K. 3550), cf. *AM.* 21, 1 (K. 6196).

Obverse.

1. [If a man's head hurts him], his mouth pricks him, his eyes trouble him, [his ears sing], his throat chokes him, his neck-muscles hurt him, . . . his fundament, his breast, his shoulders and his loins hurt him, [his fingers] are cramped, his stomach is inflamed, his bowels are hot, . . . his hands, his feet and his knees ache,⁶ he has . . . , either his bowels are affected, or his kidneys are upsetting him, . . . or he is sick of retention, either restriction of constipation or restriction of breath . . . , or is sick of nephritis(?)⁷ or is sick of bile, or is sick of jaundice, . . . [or] is sick from a curse, or is sick of ulcers(?), or of rheumatism, or of the hand of a ghost, . . . or is sick of the demon "Raiser of the Head for Evil". . . . To assuage his obsession⁸ . . . poppy, "stone" of poppy (opium), *Artemisia*, **balsam, **sagapenum*, . . . licorice, root of licorice, male *Mandragora* . . . [*kan*]*kadu*, sumach, *lidrušu*, *Salicornia*-alkali, . . . fennel, fennel-root, *šašumtu*, **Arnoglosson* . . . *Solanum* . . .

Reverse.

3. . . . gum of *galbanum, turmeric . . . , . . . (?) into his nostrils [thou shalt blow, and he shall recover].

6. . . . pine-turpentine, hellebore, a plant for pain(?) . . . together thou shalt pound, with *uša*-beer and . . . thou shalt mix, . . . , [in] rose-water he shall wash, with oil of fir-turpentine thou shalt anoint, [and he shall recover].

¹ [*I-ka*]-*la-šu*, cf. 22, 2, 4.

² *Innapaḫū*.

³ *Ir-ru-šu ia-ru-ru*, cf. 43, 5, 8, *irrušu iarrur*.

⁴ *Muḫḫu*.

⁵ *Tēn-šu iltana* . . . (from *šanū*).

⁶ *Ikaṣṣašu*.

⁷ *SA.HI.BIR*, probably connected with *SA.HI.RA.ṢA* = *rapadu*, a disease (Br. 3143) (cf. *AH.* 83, 258). As *BIR* = "kidney" we may probably see some kidney trouble here.

⁸ *Ana maš-tak-ti-su bulluḫi*. *Maštaktu* is said of eight colossi, each of 4610 talents, *maš-tak-ti eri nam-ri* "(with) overlay (?) of bright copper" (Sargon, *Khors.* 162), (? *𐎶𐎶𐎶*, Pu. "be overlaid with rust"). The lion-heads found by Dr. Hall at El-Ubaid will bear this out. The word occurs also with silver in the difficult proverb (Jäger, *BA.* ii, 286 fl.) *simme la asa bubuta la akala maštaktum kaspi u mašarru ḫuraši silimta ana nadani bubuta ana pašari ikkalá*. The Sumerian equivalent here is *GIŠ.KI.LAL*, and *KI.LAL* = *sanaḫu ša šarpi*, i.e. "pressing of silver" (overlay or inlay?). *KAR.* 70, 5, gives *INIM.INIM.MA maš-tak-ti [lib]* *ZI.GA* (for the restoration see rev. 22). A root *𐎶𐎶𐎶* is found, used of ears (*šuttuḫa*), and finger-nail (*šuttuḫat*) (Dennefeld, *Geburts.*, vocab., "beschädigt").

9. . . . *ammi, pine(?), *Salicornia*-alkali, hellebore, fir-turpentine, pine-turpentine, thou shalt mix [together], apply(?),¹ and he shall recover.

11. . . . fir-turpentine, pine-turpentine, mustard, seed of *ḫutru* . . . these drugs thou shalt pound (and) strain; parched *Lolium* . . . in a pan thou shalt mix, spread on vellum, anoint him (*sic*) and he shall recover.

14. . . . alum(?), *asa foetida*, *storax, pine-turpentine, fir-turpentine, . . . together thou shalt pound, strain, in kidney-suet of a male sheep, wax(?) . . . at his anus apply: an enema² besides . . . hellebore, *ammi, *mint, *asa foetida*, . . . *suadu*, seed of . . . (*remainder mutilated*).

22. (*Dup. of AM. 41, 1, iii, 22?*) . . . fir-turpentine, pine-turpentine, roses, *Lolium*, . . . mustard, *mint, *ammi, saffron, . . . fourteen drugs in beer (and) vetch³ water . . . [at his anus] thou shalt pour.

D. DISEASES OF THE MOUTH.

The series *Šumma amelu šinnēpī-šu imarašuvī* ("If a man's teeth ache") is a short series, apparently only of two tablets, probably preceding in order the series *Šumma amelu pū-šu ikabbīt*.

¹ *Te* (?) - *pu(sir)* - . . . (?) - *ma*.

² NAGAR (Br. 11163) must be *allanu*, as Ebeling, *Arch. xiv, 35*, saw, recognizing the meaning ("zäpfchen"). Cf. *AM. 43, 1, 6*, "these six drugs NAGAR-*nu šamru* are a powerful NAGAR-*nu*," while ll. 4, 10, 18, speak of making an *al-la-na(an)* (for his anus). 74, 1, 33, speaks of kneading roses, fenugreek, and *Lolium* in rose-water, binding it on, mixing in oil, making a NAGAR, putting it to his anus; 57, 1, 6, of mixing certain drugs in oil, making a NAGAR-*nu*; 25, 5, 5, of mixing drugs in oil, NAGAR-*an ša* . . . Kū. iii, i, 49 . . . *išteniš HAR.HAR ina lipi tuballal NAGAR-*nu teppuš(uš) šamni tasalaḥ ana ku-šu tašakam*, i.e. grind together . . . , mix in fat, make an *allanu*, sprinkle with oil, put to his anus. On the other hand, 53, 9, 7, speaks of the patient having . . . and (it) pouring blood, . . . *ammi, *Lolium*, alkali . . . thou shalt make an [*alla*]na, put to his anus; 47, 1, 2, for trouble in which sleep is concerned, for his recovery bray mandrake and *chamomile, mix in oil, make an *al-la-na* . . . ib. 4, for something similar, "that man Kū.GIG (anus trouble) . . . , Kī.KAL of dates, Kī . . . , make an *al-la-na* . . . "; 53, 11, 7, " . . . Kī.KAL of dates pound, [make] an *al-la-na* "; 58, 9 r. 3 . . . *al-la-nu* Kū.GIG (cf. ll. 6, 8); 43, 1, 18 . . . "dates of Dilmun thou shalt mix, an *al-la-na* . . . "; 5, 7, 6, . . . Hī *al-la-na kak-uš*; 101, 3, iv, 7, [*al*]-*la-na kak-uš* Nī 'erini šud ana ku-šu tašakan(an)-ma ina-eš; 50, 6, 6, . . . *tabašal (šal) tušešd(a) al-la-na* . . . ; 57, 5 r. 6 ff., *ammi, *mint, *asa foetida*, roses, *Lolium*, opium, salt, *Salicornia*-alkali, suet of the kidney of a male sheep, these ten drugs *al-la-an teppuš(uš)*; 43, 1, 7, " *ammi, hellebore, *Lolium*, (?), *storax, *asa foetida*, alum, fir-turpentine, [pine]-turpentine, myrrh, gum of andropogon(?), salt, these twelve drugs separately thou shalt pound . . . boil in fat, wax (and) [gum] of *galbanum, mix, an *al-la-an teppuš(uš)*, [at his anus] apply, and he shall recover." Cf. also 43, 1, ii, 6; 81, 9, 6; 96, 2, 2. Medically it is obviously an "injection", "clyster", "suppository"; philologically it may be from *elēlu* "be pure", with -*anu* attached, lit. a purgative, parallel to *κλύσμα* or "drench". Note the similarity of *SM. ii, 507*, and also the suppository *KAR. 201, obv. 45*, . . . *lu ina lipi tuballal ubani teppuš(uš) ana k[u-šu tašakan]* (cf. also rev. 17, 18) " . . . or in fat thou shalt mix, a 'finger' thou shalt make, put to his anus", such as would nowadays be made of soap for a baby; cf. *JRAS. 1924, 456*, *allan šerri* "an *allanu* (enema) for a baby".*

³ A.ŠA.HAR.RA : ŠE.GU.ŠA.HAR.RA, obviously one of the vetches (*AH. 278, Vicia spec. impr. Ervilia*); "water of vetches," like "water of lentils", *AH. 114*.

Tablet I.

No. 65. *AM.* 23, 6 (S. 234); *AM.* 24, 2, and 25, 2 (K. 10330 + 79-7-8, 34), probably part of 68, 5 (K. 11753); *AM.* 25, 9 (K. 16401); *AM.* 28, 1 (K. 2439 + 2849) + 30, 8 (K. 2479) + 25, 1 (K. 7635) + 30, 10 (K. 13407).

Col. i.

1. (*AM.* 28, 1.) If a man's teeth hurt, thou shalt take a *mušdimgurinna*¹ . . . , the white of its inside thou shalt enclose in wool, with oil [sprinkle(?), put it on his tooth]; male mandrake-root, *ammi-root, . . . *storax, gum of *galbanum, vinegar, . . . flour² against his mouth (tooth) [thou shalt bind and he shall recover].

6. Powdered alum, . . . *galbanum, dates . . . , juice (tops) of *Crataegus azarolus*(?) . . .

9. *Hi*- . . . -plant, . . . powdered alum(?) . . .

(After a gap of about 10 ll., *AM.* 30, 8.)

(*AM.* 30, 8.) 4. If ditto, for one day thou shalt rub . . . If ditto, flour of dust of millet . . . he shall pour³ . . .

7. (*Dup.* of *AM.* 30, 13, 6.) If a man's tooth hurts him . . . If ditto, a green (yellow) frog . . . If ditto a green (yellow) frog . . .

(*AM.* 25, 9, K. 16401, is probably the left-hand lower corner.)

(25, 9.) 2. If a man's mouth . . . thou shalt roll, sprinkle with oil . . .

4. If ditto . . .

5. If ditto . . .

6. If ditto . . .

7. . . .

8. If ditto . . .

9. If ditto . . .

(Col. ii is unidentified: it might possibly be *AM.* 27, 9, K. 13385, an incantation for "When blood comes into a man's mouth". Except for this text of Col. iii the beginning is lost until we reach 25, 1, iii, 1 ff.: l. 10 "Incantation for Toothache". An incantation begins with ll. 11, 12, and after a gap of about 3 ll., 28, 1, iii, joins. After two ll. of ritual comes an incantation, 28, 1, iii, 4-7 + 30, 10, 1-4, and 24, 2, 1-6, and then another ritual and incantation which can be nearly completed from 24, 2, 7-15, and 28, 1, iii, 7-13 + 30, 10, 5-10 as follows:—)

¹ See No. 34, l. 4.

² *Upuntu*.

³ *DUB - rak* = *isarraḫ*, as in Zimmern, *Rit.*, p. 223. *I-sar-raḫ*, 24, 5, 15; *ta-sar-raḫ*, 54, 1, 8, 11, of pouring or spreading either "flour of *gum (*kirkiranu*) (of pine)" or pounded *ammi on (= *ana pani*) a thorn fire to fumigate his anus. Is it שָׂרַק "spread"?

Incantation for Toothache . . . the charm [three] times over it thou shalt recite . . .

4. Charm.¹ O Shamash, because of my tooth which hurteth me [some ghost(?) (un)buried(?), to whom I have not offered food nor poured forth water, is angry; like a sealed tablet(?)² to thee I pray that I may shut him in and cover him(?) over, like a moth whose tooth hurteth him not, so shall tooth, too, not hurt me.

(Then follow several mutilated prescriptions and incantations: 28, 1, iii, 14 ff.; 24, 2, 16 ff.; "Incantation for Toothache . . . in the morning [thou shalt recite] the charm three times . . .

Charm. After Anu [made(?) . . . (and) . . . made Eridu?], Eridu made GI . . . like the star(s) a number [had not?] . . . , harm(?) . . .

Incantation for Toothache . . . [thou shalt tie a *patinnu*³-bandage], as [thou tiest] the bandage [the charm thou shalt recite], put it on his tooth and . . .

Charm. Anu . . . , after Anu made . . . "

The text then breaks off, but 25, 2, 1-4, may supply the completion (Col. iv) with "[The charm is] not ya-tu, it is the charm of (such and such a god)". 25, 2, 5-13 supplies the ends of lines of the next portion, and then comes the Legend of the Worm, CT. xvii, 50; AM. 23, 6, 1 ff.; 25, 1, iv, 1 ff., and 2, 15 ff.:—

Incantation for Toothache.

Charm.⁴ After Anu made the heavens, the heavens made the earth, the earth made the rivers, the rivers made the canals, the canals made the marsh, the marsh made the Worm. The Worm came weeping unto Samas, (came) unto Ea, her tears flowing: "What wilt thou give me for my food, what wilt thou give me to destroy?" "I will give thee dried figs (and) apricots." "Forsooth, what are these dried figs to me, or apricots? Set me amid the teeth, and let me dwell in the gums, that I may destroy the blood of the teeth,

¹ This must be thus restored: Šiptu. ^uŠamaš aš-šum šinni-ia ša ik-kal-an-ni . . . -bi-ru (✓ קבר?) ša ki-is-pa la ak-si-pu-šu u me-e la ak-ku-šu [. . .] it-taš-bi-is ka-ni-i[g(?)g]iš(?) ka-a-ša am-hur-ka ak-ta-la-šu u ak-ta-at(?)ma(?)š-šu(?) kima a-ša-ši šinni-šu la ikkal-šu a-a-ši šinnu la ik-kal-an-ni.

² Or "a sealer (of tablets)".

³ *Patinnu* = *parsigu*, particularly "head-bandage" (MA. 835). Cf. in 45, 5, 5, XIV KU pa-tin-ni tu-kap-pat "thou shalt tie together (קפת) fourteen bandages" for stomach-trouble, i.e. to swathe the man's stomach. *Kapātu*, PRSM. 1924, 23, n. 7.

⁴ This text has been previously translated in my *Devils*, ii, 160; *Semitic Magic*, xliii; Meissner, *MVAG*. 1904, 74. AM. 25, 2, 15, allows us to restore l. 1 ul-tu ^uA-nu ib-nu-u same(e).

and of the gums chew their marrow.¹ So shall I hold the latch of the door."
 "Since thou hast said this, O Worm, may Ea smite thee with his mighty fist!"

Incantation for Toothache.

Ritual for this: thou shalt mix *usa* (-beer), (of ?) millet-meal² and oil together, repeat the incantation over it three times, put it against his tooth (mouth).

Charm.³ Be long,⁴ (yet) we shall (surely) catch thee! The door is the flesh, the latch is the bone; she hath entered [the flesh], she hath lifted the bone, she hath bitten the flesh, she hath dug into the bone; she hath brought decay⁵ into the teeth, she hath [brought] fire unto the latch(?)! Whom shall I send unto Marduk, the eldest son [of the Deep], that he may bring a drug for the charm for recovery until . . . ?

The charm is not . . . (?); it is the charm of Ea and Marduk, the charm of Damu [and ?] Nin-ka[r-rak]. O Gula, [quicken] the recovery! . . . Recite the Charm.

Incantation for Toothache. The ritual not written.

(Catch-line.) If a man's teeth are all loose.⁶ First Tablet of the Series "If a man's teeth ache".

Tablet II.

No. 66. The *Second* Tablet of the Series is (apparently) made up of the following: (1) *AM.* 36, 2 (K. 2419) + 21, 1 (K. 2461) + 31, 6 (K. 3303) + 23, 7 (K. 8169) + 28, 4 (K. 10733) + 27, 5 (K. 11630) +

¹ Here the Kouyunjik versions end. Read *uk* for my *az*, *AM.* 25, 1, 7; *luksus kusasē-šu*, Meissner "will ich ausbrechen seine Zähne"; Holma, 24, "Zahnwurzel?"; but *luksus* must be from 𒌦𒌦𒌦 "chew", and *kusasē* a form of 𒌦𒌦𒌦𒌦𒌦, *cartilago, pars ossium medullosa quæ mandi possit* (Payne Smith, 1786). In l. 15 of the Bab. version of *CT.* xvii, we must obviously correct the scribe's *šu-uk-ka-an-ni* (see the photograph) with *AM.* 23, 6, 4, [*š*]u-uk-na-an-ni.

² *AH.* 203. Cf. Hrozný, *Getr.* 150, KAŠ.U.SA.ZIZ.AN "Emmermischbier". Or is 𒌦𒌦𒌦 "bloom" here?

³ The composite text runs (28, 1, iv, 2 ff.; 25, 1, iv, 10 ff.; 23, 6, 8; cf. also 36, 2, iii, 1-3):—

Šiptu. A-ri-ki ni-ba-(a)-ri-ki ^{1u}daltu šēru ^{1u}sikkuru GIR.PAD.DU [*šēri*]e-ru-ba GIR.PAD.DU iš-ši iš-šu-uk šēri iḫ-r[i] GIR.PAD.DU a-na šinnē^u it-ta-di i[k]-ki-ta (sic, re-examined) a-na sikkuri (?) [it-ta (?)]-di iṣati. Man-nu lu-uš-pur a-na ^{1u}Marduk mār riš-ti-i [ša apsi lu-(so also S. 234, not ki)]-še-bi-lam-ma šammi šip-ti (v. *šipti*) TIL.LA.NA a-di . . . TU ul ya-at-tu šipat ^{1u}Ea u ^{1u}Marduk šipat ^{1u}DA.MU [u ?] ^{1u}NIN.KA[R.BA.AK] ^{1u}Gu-la TIL.LA-ma [ša-ba-ki bulluṭi(i)] TU.EN. (^{1u}NIN.KA[R.BA.AK] appears certain.)

⁴ A threat in the imperative, not unlike the Hebrew, e.g. Is. viii, 9. It is better thus than to take *ari* from *aru* "I shall reach thee".

⁵ *Ikkitu*, cf. *PRSM.* 1924, 2, n. 5, where it means "scabies"; compare also *rišutu* in the same connexion, and again as caries in n. 2 of No. 66.

⁶ *I-na-aš-šu* from *nāšu* "quake".

45, 7 (K. 13900) + 28, 3 (K. 13971) + 66, 10 (K. 16408) + 27, 1 (K. 16411) + 39, 2 (K. 16418) + 26, 9 (Rm. 944); (2) *AM.* 26, 2 (K. 3267) + 25, 6 (K. 8089) + 23, 10 (K. 8956) + 23, 1 (K. 9072) + 26, 8 (K. 9438¹); (3) *AM.* 90, 2 (K. 2290); (4) *AM.* 26, 6 (K. 6166). Although these four component pieces have no actual contact, there is very little doubt that they once formed part of the same tablet.

Col. i.

(*AM.* 21, 1.) 1. [If a man's teeth] are [all] loose and decay² [sets in] . . . [thou shalt rub] . . . on his teeth until³ blood comes forth, [and he shall recover].

3. [If a man's] teeth are loose and . . . , . . . (and) *ammi thou shalt bray together, r[ub on, . . . and he shall recover].

(Then follow the beginnings of fourteen lines, and then begins *AM.* 31, 6) :—


20. . . . myrrh, . . . , *opopanax, these eight drugs . . .

23. Savin(?) (or tragacanth?), pine-turpentine, . . . , *asa foetida* . . .

(Here are joined *AM.* 28, 4 + 26, 9.)

25. If a man's teeth have become⁴ yellow, his mouth . . . him, . . . , thou shalt bray together "salt of Akkad", *ammi, *Lolium*, pine-turpentine; (with these) with thy finger [thou shalt rub his teeth] . . . , cleanse his mouth and nostrils . . . , wash his mouth with honey, oil (and) *kurunnu-beer* . . . with a feather thou shalt make him vomit,⁵ and (then) thou shalt

¹ This last join due to Ebeling, *Keilschr.* 42.

² *Rišutum*, itch in head, *PRSM.* 1924, 2, n. 5. The extension of meaning is seen in  caries.

³ Read *adi*, not *kab*. Re-examined.

⁴ *RU.A.*, lit. "fall".

⁵ *Ina* *id* (= *kappi*) *tušaprašu*. The credit of this translation belongs to Ebeling (*Arch.* xiii, 11, n. 3, K. 2414, K. 3516, my *AM.* 80, 1, 15) "mit einem Flügel(?) sollst du ihn zum Erbrechen bringen", quoting *id* = *kappu* (*SAI.* 4692). *MA.* 420, *šubat kappi* "garment of feathers" is comparable. He does not, however, give any further explanation of *tušaprašu*.

His ingenious explanation is now confirmed by *AM.* 21, 6, 5 . . . *ga-pi* (i.e. *gappi*) *tušaprašu*, and *AM.* 36, 2, 7, *ina id* *tu-ša'-ra-šu*. The latter word appears to be a variant for *tušaprašu* (*AM.* 80, 7, 6 and 9 and 11); it was first noted by Kū. (iii, i, 16, *BI.A.SUD išatti tuša'-raššu*; cf. ii, 25). He connected it with ערה "entleeren" (as meaning "erbrechen und cacare?" p. 139), including *iarru*. Kūchler's meaning for this seems undoubtedly correct; it implies evacuation or getting rid of the trouble by ejection in some form, but I think it is rather from פרו "throw", "shoot". The following examples show the use of *ina id tušaprašu*: *AM.* 45, 1, 5; 48, 2, 24; 49, 5, 4; 53, 10, 3; 55, 7, 3; 80, 1, 15; 87, 8, 4.

Iarru is added after the patient drinks nettle-seed in hot rose-water for a cough (80, 1, 11, cf. *SM.* ii, 670, 204), *storax in beer (36, 2, 8), castor oil in beer (36, 2, 10), the first instance indicating the breaking up or expulsion of phlegm, the last the natural result of castor oil. In Kū. iii, i, 52, *iarru* is added after ". . . fennel, *storax, *manna, **Ricinus*", which would produce the same result. In iii, ii, 23, Kūchler rightly considers that vomiting is indicated: *Šumma amelu ina patan riš libbi-šu ikašassu* (see No. 64, n. 6) *išata libbi irtaši ina giši-šu marta iarrum* (während er rülpet, Galle entleert).

bray lupins (and) turmeric together, [let him drink (them)] in oil and *kurunnu*-beer, [and he shall recover].

29. Crushed(?)¹ potsherds thou shalt reduce, bray: cleanse his mouth and nostrils; let him draw up² oil by a reed-tube into his nostrils, the potsherds(?)³ with wool . . . thou shalt pound fine, put into his nostrils.⁴

31. If ditto, thou shalt bray the plant *kak.sik*(?),⁵ in oil [thou shalt mix] . . . fill(?), and he shall recover.

32. If ditto, thou shalt boil gum of the *Aleppo pine with honey . . .⁶ of his mouth it shall remove.

33. (*Here is joined AM. 66, 10.*) [If] . . . , [fat] of male sheep thereon(?) . . . , he shall scrape⁷ his [teeth], . . . thou shalt cleanse,⁸ the black of his teeth it shall remove.

35. . . . together thou shalt bray, apply to his mouth (tooth).

36. . . . thou shalt put and he shall recover.

Here almost certainly follows, after a short interval, AM. 23, 10 + 26, 8 (etc.):

1. If a man . . .

2. If a man . . .

3. Seed of . . . he shall pour(?) . . .

4. Seed of oak (= galls) . . . ; then refined oil . . .

5. Roses . . . thou shalt put; then refined oil . . .

6. If a man's tongue *ip*- . . . , [juice (tops)] of tamarisk, juice (tops) of lemon, juice (tops) of *Solanum*, juice (tops) of . . . thou shalt dry, pound (and) strain, on his tongue anoint curd, (then) put it on his tongue and he shall recover.

¹ Re-examined. *Adiṣti* appears certain (*adābu*, HWB. 20).

² *GID-da*, i.e. *iṣadada*; cf. 55, 3, 8, and 64, 1, 10, *GID-ad*.

³ *Ha-an-ša* - [ab ?]-*ti* (?); cf. *ḥanṣabu* "potter"; but restoration doubtful.

⁴ Read . . . *ti itti idḫi tudakkaḫ ana naḫiri-šu tašakan*.

⁵ Re-examined, and apparently thus.

⁶ [*Ki*]-*bit* "heaviness, pain" ?

⁷ *Ugarad*, 𐎶𐎵𐎶𐎵.

⁸ Re-examined. Probably *ta-kap-par*.

8. If a man's lips [are cracked?] . . . , thou shalt bray **Ferula communis*(?) in anointing¹ oil, (and) anoint his lips, applying² (it) thereon on tow,³ and he shall recover.

9. If ditto, arsenic⁴ (and) myrrh in oil thou shalt bray, anoint [and he shall recover]. If ditto, and the blood has formed a scab(?),⁵ to remove the scab(?) thou shalt repeat it (i.e. the above treatment), anoint the affected surface with curd, *storax [thou shalt apply, and he shall recover].

11. If ditto, thou shalt mix myrrh in wax, anoint his lips, [and he shall recover]. If ditto, his lip being broken,⁶ thou shalt fill it with unmelted wax⁷ and he shall recover.

13. If it is broken(?), thou shalt bray pomegranate, (and) *kamkadu*-plant, ditto; (or) a *Scolopendra*⁸ in curd [thou shalt bray, ditto].

14. (Here are joined AM. 25, 6 + 26, 2.) . . . its head⁹ . . . *storax thou shalt apply, the affected surface thou shalt [anoint?] . . . three times thou shalt do this and he shall recover.

17. . . . powdered alum, myrrh . . . [into his nostrils by a reed]-tube thou shalt blow, he shall recover.

19. [Incantation for] the Mouth.¹⁰ As before.

20. . . . *ammi(?) alum, roses, gum of *Andropogon*(?) . . . thou shalt introduce¹¹; into his nose a *kattilu*¹² thou shalt put; *Salicornia*-alkali . . . , *ammi, thou shalt mix, inside his nose thou shalt rub.¹³

¹ See No. 33, 4.

² *Tuṭappa*, 𐤠𐤕𐤕𐤐 in Pael. Cf. p. 47, n. 1, and PRSM. 1924, 27, n. 1.

³ GI.ŠA.GI = *puḫlu* and *ḥandū*, the latter being *šim-šim ša libbi ḫanēvi* (Br. 2516), either "pith" or the fluff from the heads of bulrushes used by potters for stiffening their clay (JRAS. 1923, 239). *Puḫlu* 𐤐𐤕𐤕𐤓 (given as the seed-capsule of flax) will probably be "tow", the coarser fibres of the flax-stalks.

⁴ For arsenic on cracked lips, cf. SM. ii, 668. See No. 36, iv, l. 12.

⁵ *Iṣanāḫa*, *ṣinnaḫti*. Br. 10584, KU.BAR.RA = *ṣubat cluti* ("upper garment"), and SAI. 8040 = *ṣanāḫū*; presumably the outer crust formed by the dried blood. *Ana ṣinnaḫti nisi* (u) *tutar-šum*, cf. AM. 37, 2, 7, with 35, 1, 8.

⁶ *Hipāt*, here like *hibi* referring to a broken place in a tablet.

⁷ *La balla*.

⁸ *Adudailu*, Delitzsch (Stud. 1874, I, 76) 𐤠𐤕𐤕𐤓 "millepede". On a *Scolopendra* (exceeding three inches) at Mourad Pasha, v. Chesney, Exp. i, 726.

⁹ Sic probably.

¹⁰ Cf. 23, 7, 8.

¹¹ *Tu-lam*, cf. VR. 45, ii, 24, *tu-la-a-ma*. Used with alum (16, 5, ii, 7), presumably *šv.sr a-bar* ("a finger of antimony") (101, 3, iii, 14), wax (75, 1, 21). The Syr. 𐤠𐤕𐤕𐤓, *appropinquaret*, may offer a solution. *Tulamnam*, 25, 6, ii, 6, see p. 66, n. 4.

¹² Read thus.

¹³ *Taktanar*, 𐤠𐤕𐤕𐤓, see PRSM. 1924, 18, n. 2.

23. [If a man's nose . . . has been stricken,¹ and it collects . . . (?)² [for] his [recovery ?] thou shalt mix *mint in cedar-oil and inject it into his nostrils.

25. [If ditto, alu]m(?), myrrh, *storax, thou shalt bray together, apply thereon and he shall recover.

26. . . . thou shalt bray, bind thereon, and he shall recover.

27. . . . a pearl which a priest³ . . . [into] his nostrils thou shalt blow, . . . these two drugs.

Col. ii. (*Here is AM. 27, 5, rev.*)

4. . . . and he shall recover :

5. . . . cinnabar thou shalt bray, bind . . .

7. (*Here are joined AM. 27, 1 + 28, 3.*) [If a man's mouth(?)] . . . thou shalt bray pomegranate . . . [If ditto(?)] thou shalt bray myrrh . . .

9. [If ditto], and in his nostrils . . . thou shalt cleanse his nostrils . . .

11. If a man's nose and mouth hold foetor, . . . thou shalt roll up a linen pledget, bray *Salicornia*-alkali(?), powdered alum, . . . , *ammi, alum; sprinkle the pledget of linen with oil . . . *manna(?) green thou shalt bruise, five shekels of . . . thou shalt let him drink and . . . in oil and beer he shall drink . . . ; . . . thou shalt bray, in oil and beer he shall drink; . . . thou shalt reduce, bray, [mix] in oil, let him [dr]ink, and he shall [recover].

19. (*Here are joined AM. 39, 2 + 45, 7.*) [If a man's mouth hath] foetor . . . and his stomach . . . gum of *Andropogon*(?) thou shalt bray in oil and beer [he shall drink, and he shall recover].

21. . . . alum(?) thou shalt bray, in oil and beer he shall drink, [and he shall recover].

22. . . . mercury⁴ thou shalt bray, in oil and beer he shall drink, [and he shall recover].

23. . . . alum(?) thou shalt bray, in honey and beer [he shall drink, and he shall recover].

¹ RU.RU.

² *Ni-pil* (*bil, ne, kum*) - *ma-tu up-ta-na-har* (or *tu-up-ta-na-har*). For the remedy cf. *SM.* ii, 67, for the "foetid nexus"; "take moist calaminth, and pound it, and squeeze out the juice, and inject it into the nostrils."

³ *anNisakku*, as it stands.

⁴ Mercury is a glandular stimulant, *P.* 601.

24. (Here is joined AM. 36, 2.) [If a man's . . .], his heart burns, his saliva¹ comes, foetor attacks him . . . , thou shalt mix . . . in water, bind (it) on his head.

26. [If ditto], thou shalt weigh out (?) [in equal quantities ?] *Nigella*, *ammi, *Eruca*, arsenic trisulphide, powdered alum, *storax, (and) bray (them) : thou shalt rub a paste (?)² of dough on the root of his tooth [until] blood comes forth ; (then) these drugs thou shalt apply to his tooth,³ and he shall recover.

29. [If ditto, and his . . .] does not stop, a quarter of a shekel of gum of *Andropogon* (?) in oil and *alappani*-beer [thou shalt mix], blow [into] his [nostrils ; with a feather thou shalt make him vomit, and, after this, *mulutinna* beer he shall drink and he shall recover.

31. [If ditto] . . . *storax thou shalt bray, he shall drink (it) in beer, evacuate and he shall recover.

32. Thou shalt bray powdered alum (and) apply it to his tooth^{3,4} ; let him lick the upper stone of a *Lolium* mill, and he shall recover.⁵

33. (Here is joined AM. 26, 9.) **Ricinus* thou shalt bray, he shall drink (it) in beer, evacuate, and he shall recover.

34. Thou shalt slit a leek, rub on the root of his tooth, and he shall recover.⁶

35. *Ammi, *Lolium* thou shalt bray, he shall drink (them) in beer, evacuate⁷ and he shall recover.

36. *Nigella* thou shalt bray, in beer ditto.

37. Powdered alum thou shalt bray, he shall drink (it) in beer, evacuate, and he shall recover. . . . alum thou shalt bray, ditto : *manna thou shalt bray, ditto.

39. . . . thou shalt reduce . . . into his nostrils thou shalt blow.

¹ *Illatu*, see No. 70, l. 2.

² *Humbizate*, doubtful : *خبز* ?

³ Or "mouth".

⁴ For alum for teeth, cf. *SM.* ii, 667.

⁵ See No. 70, l. 16.

⁶ Cf. *AM.* 30, 2, 2. For leeks to cure gangrene of the mouth, see *SM.* ii, 668.

⁷ *HAL*, similarly in l. 14 ; see also *AM.* 83, 4, i, 6, 8, 9, 11 ; *SAI.* 33 ; *HAL* = *ard*, and cf. *Kû.* 108, 139.

41. . . . three times . . .

(Here must be placed in continuation AM. 23, 1, and AM. 90, 2, obverse, the latter coinciding with AM. 23, 1, in divisional lines, without actually joining.)

2. Pyrites,¹ skin² of (the fruit of) the plant . . . , powdered alum [thou shalt bray, in] beer he shall drink.

4. If a man [has] foetor, he shall drink . . . in beer. If ditto (2) [he shall drink] *manna in oil and [beer]. [If ditto (3)], ditto . . . If ditto (4), [ditto] *ammi (and) . . . [in oil and beer(?)]. [If ditto (5)] . . . ditto. If ditto (6), he shall drink lupins . . .

8. If a man's mouth [has] foetor, . . . thou shalt take(?): alum(?), *ammi, . . . *urpana*(?)³ *storax, *annuḫa*[ra] . . . , crushed flour, the smell of his teeth thou shalt . . . , these drugs thou shalt apply.

12. If ditto, [thou shalt bray] powdered alum, he shall drink [in] beer. If ditto (2) [thou shalt bray] powdered alum, he shall drink [in] pressed grape-(juice). If ditto (3) [thou shalt bray] *ammi, he shall drink [in] pressed grape-(juice). If ditto (4), . . . , *ammi(?), he shall drink in oil and beer. If ditto (5), thou shalt bray powdered alum, [roll up a pledget of linen] (which) thou shalt sprinkle with oil, gather⁴ up the alum (in it), put it [in] his [nostrils], let him starve himself for one day, and when the daylight shines forth, let him cook(?) . . .⁵ (and) eat.

18. When a man's mouth and nostrils hold foetor, [thou shalt bray] [alum], roll up⁶ a pledget of linen, sprinkle (it) with oil, gather up the alum (on it), [put it] in his nostrils; with pounded powdered alum . . . (?)⁷ thou shalt rub his nostrils until blood appears. [Thou shalt do] this for three days: on the fourth *manna, green⁸ thou shalt press (and) take its juice, two shekels of oil [add, apply, and] he shall recover.

¹ *Mar* (?) - *ḫa-ši*, see my *Chemistry*, 117.

² *BAR* = *ḫuliptu*, see p. 44, n. 1.

³ See 19, I, 5.

⁴ *Tulamam*; cf. the similar passage in I. 20. *ṣ* = "gather together".

⁵ For this line read *ānu I kam liš-bar*(or *bir*)-*ri-ma kima ur-ra it-tam-ra* . . . [*lib-l*]*a-šal ikkal*.

⁶ *Ta-ṣap-par* (*ṣap* on re-examination clear).

⁷ *Lu-ba-ri-e*, translation doubtful.

⁸ *gīl* (AH. 160) = properly *manna; *Gil* is the tree from which it comes (= *ataru*, *ṣ*), oak). "Gall-nuts" are common in the equivalents in SM. ii, 68 ff. The drug here necessary is the styptic provided by the oak-galls (tannin).

23. If ditto,¹ thou shalt bray alum, thou shalt roll up a pledget of linen, [sprinkle (it) with oil, gather up the alum (on it)], put it in his nostrils; *storax, *ammi in equal parts(?) [thou shalt bray, mix], apply to [his . . .]; thou shalt cleanse his mouth and nostrils . . . thou shalt press [*manna(?)] green, squeeze its juice, 1 *bur* of oil [thou shalt add, apply and he shall recover].

27. (*Here is AM. 26, 2.*) If ditto . . . thou shalt bray together, in . . . in *hibṣi*² . . .

Col. iii (*here is AM. 26, 6.*)

3. If ditto . . .

4. unto . . .

5. 1 *bur* . . .

6. If a man's mouth . . .

(*Approximately here are ll. 1-2, AM. 90, 2, reverse.*)

3. . . . thou shalt dry (and) bray . . . , thou shalt cleanse, and he shall recover.

5. (*For a similar receipt see Col. ii, 11.*)

Ll. 11-22 mutilated. Then after a hiatus of about 20 ll. *AM. 36, 2*, reverse.

1. . . . the bolt . . . hath cast³ . . . As an untimely birth⁴ taketh not the breast of [its] mother, [so shall the . . . not . . .] unto thy *siptu*. [The charm is not . . .], it is the charm of Ea and Marduk, [the charm of Damu] and Gula, [the charm of Nin-aḥa-kuddu], the mistress of charm. [O Gula], mistress of life, quicken [the recovery, . . .]. Charm.

11. [Incantation for when] foetor seizes on him.

12. . . . [in] beer let him drink and he shall recover.

(*Eleven lines lost almost entirely.*)

(*Here must be 27, 5, duplicate of obv. 54, 3, 1-11.*)

¹ Cf. *AM. 28, 3, 6 ff.*

² *Hibṣu*; also 33, 1, 10, after fumigation; 105, 1, 13, and its dup. 35, 5, 5, where after his head has been anointed with cedar-oil, he is to eat *hibṣa* with lolium. It may be מִשְׁחָא "mash", or *hibza* خبز "bread" (*AH. 128*).

³ Cf. the previous text, Col. IV, towards the end.

⁴ *Nid libbi*, Holma, 109, *nit libbi* "womb", but the sense demands "untimely birth" (as Thureau-Dangin, *RA. xix, 82*); cf. *CT. xxiii, 10, 16*, *AN.KÙ.BU* in the parallel passage. Cf. *nidu*, perhaps a mock-sun, lit. "a casting" (see my *Reports, ii, xxvii*).

2. [Charm. It] rageth¹ like a lion, although(?) not² a lion . . . , [it] . . . like a panther(?)³ . . . , [it is fierce ?] in wrath, it uttereth . . . [Whom shall I] send to the daughter of Anu of [Heaven], that they may bring me their ewers of silver,⁴ and their basins⁵ of [gold, that they may gather me] the waters of the Eulaeus, the waters of the broad sea, [wherein] no woman in her courses hath washed her hands, [wherein] no [unclean woman] hath washed her clothes, [wherein no unclean(?) man] hath brushed(?)⁶ his hands

Col. iv (*here must be AM. 26, 6*).

that they may draw up (the water), . . . ,⁷ that they may put the water in his mouth, and the *um*(?)-*mu*(?) . . . , the *labātu*(?),⁸ the foetor⁹ be removed(?). Recite the charm.

3. Incantation for when foetor seizes on him.

4. If ditto, alum, *ammi, thou shalt bray, in honey mix, recite the charm seven times thereon, cleanse his mouth, and he shall recover.

6. . . . *ammi, . . . (?) thou shalt apply,¹⁰ . . . *ammi in beer he shall drink, and he shall recover.

8. [If ditto], *mint, *storax, . . . rue, myrrh, "Akkadian salt" . . . [thou shalt introduce(?)] (into) his mouth and nose, it shall take the foetor away.¹¹

11. [If a man's mouth(?)] is sick with [foet]or(?), one grain of fir-turpentine, . . . [one grain] of *ammi, one grain of *Lolium*, one grain of *Nigella*, . . . [one grain of asa foeti]da(?) thou shalt reduce, bray, in oil and beer he shall dri[nk, and he shall recover].

14. . . . [a man's] lip or(?) . . . where the blood . . . three days . . .

¹ [*Is*]-*sa-mir*, i, 2, of *šamāru*.

² *Ina* (?) *la*.


³ *Ništinu*; Del., *Assyr. Stud.* 33, "cat".

⁴ *Šarpi*.

⁵ *Kanduri*; cf. *PRSM.* 1924, 30; for the vessel, Thureau-Dangin, *RA.* 1920, 70, 29.

⁶ *Unassisu*; cf. *nussusu ša pirtim* (of hair), *ša zibbati* (of the tail), *MA.* 703.

⁷ *Lik-ku-mi*; or is it "black dog", with some specialized meaning, perhaps the scoop or bucket of the irrigating-machine.

⁸ *Labātu*, , *excitavit*.

⁹ Omitted in *AM.* 54, 3.

¹⁰ *Tutappa*, see No. 45, 8, and No. 66, 8.

¹¹ Not quite certain; possibly "When foetor has come into his mouth and nose".

(Large Hiatus. Then 23, 7, a charm similar to No. 26, 50, PRSM. 1924, 30, or above, l. 2):—

2. . . . Gula . . . that they may bring and . . . he may be satisfied : a seal of vitriol, seven . . . like a storm may . . . The charm is not . . . , (it is) the charm of Ea [and Marduk], the charm of Damu and Gula, the charm of Nin-aḥa-kuddu, [the lady of the charm : it is they who have performed (it) and I who have adopted (?). Charm].

8. Two Incantations for the Mouth.¹ As before. Ritual for this : thou shalt bray *margušu*-*balsam, anoint . . .

10. (Catch-line.) [If a man]'s [mouth ?] is troublesome.²

11. [Second Tablet of the series "If a man]'s teeth ache".

E. VARIOUS MOUTH-TEXTS.

No. 67. AM. 23, 2 (K. 6025; cf. K. 2418 + S. 1397, AM. 77, 1 + 28, 7, from which restorations have been made).

3. . . . Marduk the charm . . . to loose its knot, mouth-trouble . . . [Recite the charm.]

5. Incantation : if a fiend [has attacked] the mouth of a man.

6. (Dup. 78, 1, 19 + 28, 7, 16.) If a man's mouth has mouth-trouble, with **gall-apples, *ammi, mustard, he shall cleanse his mouth and drink (them) in *kurunnu*-beer and shall recover.

8. (Dup. 78, 1, 20 + 28, 7, 17.) If ditto, anemone, **Calendula*, in *kurunnu*-beer he shall drink, and shall recover.

9. (Dup. 78, 1, 21 + 28, 7, 18.) If ditto, anemone, root of **Arnoglosson* in *kurunnu*-beer he shall drink, [and shall recover].

10. Three potions³ from a text-copy of Eridu not . . .

11. (Dup. 78, 1, 10 + 28, 7, 7.) If a man's mouth has mouth trouble, thou shalt bray *Lolium* in well-water,⁴ introduce salt, alum (and) vinegar therein ;⁵ thou shalt leave it out under the stars, in the morning thou shalt

¹ Cf. AM. 25, 6, 6.

² *Šumma amelu pū-šu ikabbī* is the title of a series (see p. 57) and probably this represents the first line of the first tablet.

³ *Maškātu* (78, 1, 22, *mašgātum*) must be for *maškātu*, מִשְׁכָּאֲתוּ. Cf. NAK-an-ni *maš-ku-ti*, 92, 1, ii, 3; *maš-ki-a-ti ma-ka-lu-u*, 95, 1, 13; *maš-ki-tu an-ni-tu*, 41, 1, iv, 43; *našmādti*⁴ u *maš-ki-a-ti*, 48, 4 r. 7; *maš-ki-ta ša EN.TE.NA*, 64, 3, 6, dup. of 72, 2, 4; cf. AM. 18, 7, 10.

⁴ Cf. 76, 5, 5, "in water from the well in the Temple of Marduk."

⁵ For the *tu-ta-rab* of 23, 2, 12, the dup. has *ana* [libbi] LA RU.

wind ¹ a linen-(strip) round his forefinger, without a meal thou ² shalt cleanse his mouth [and he shall recover].

14. (Dup. 78, 1, 6 + 28, 7, 3.) If the accident of a blow on his mouth has fallen [upon him], thou shalt scoop out ³ the right eye of an *arsuppu*-fish, and the left eye of a *puradu*-fish ⁴; thou shalt put them in salt for three days, (then) take them out, and thou shalt [apply] the right eye of the *arsuppu* to the right side, the left eye of the *puradu* to the left side: with their eyes thou shalt take *asa foetida*, *liquidambar, (and) fennel, on the wool of a virgin ewe-lamb (and) the hair of a virgin kid thou shalt thread; the wool of the virgin ewe-lamb and the hair of the virgin kid thou shalt twist, ⁵ put on his neck, and he shall recover.

No. 68. AM. 23, 4 (K. 8273).⁶

1. If a man is sick of unhealthy saliva . . .

2. If ditto, *mint . . .

3. If ditto, five *bur* of *Lolium* . . .

4. If ditto, a female *Mantis* ⁷ of the field . . .

5. If a man is sick with dry ⁸ saliva . . . ***Conium maculatum*, while

¹ *Takarrak* (v. *rik*), Heb. תַּקְרַק.

² V. "he."

³ *Tuhatta*[f].

⁴ *Arsuppu*, *puradu* (see Frank, ZA. xxix, 191). The eyes must be large, and hence one of these fish may be the bizz of the Tigris and Euphrates, four feet long, sufficiently heavy to need a donkey to carry it (for a picture see Delitzsch, *Handel*, 8; description, Chesney, *Exp.* i, 739. I saw one or something like one at Mosul). The other may be the *shabbut*, a long-bodied fish with large scales, which I have seen at Carchemish. The gall is prescribed in *SM.* ii, 659 (eyes), 148 (rigidity); cf. *Tobit*, vi, i ff., of the fish which leaped out of the Tigris, and would have eaten the young man; "but as for the gall, it is good to anoint a man that hath white films in his eyes." The *puradu* (*sirradu*?) is prescribed in 82, 2, 1 (its eye); 81, 10, 2 (its gall); *KAR.* 191, ii, 9 (its brain); and a monster is represented as having the body of a *puradu*-fish "full of stars" (*Devils*, ii, 149; cf. Boissier, *Documents*, 173). I cannot identify either *arsuppu* or *puradu* with any of the twenty-two modern Arabic words for fish which I heard in Basrah.

⁵ *Tasappi*, 𐎶𐎶𐎵, *coacervavit, collegit*.

⁶ For Col. I, cf. the saliva-text, Ebeling and Unger, *Arch. f. Keils.*, i, 36, but the correspondence is doubtful. E. xiii, 17, translates this text, but I venture to offer a translation of the drugs different from his, as well as a different reading of part of the text.

⁷ *Ša-il-ti ekli*. CT. xiv, 2, K. 71, A, iii-iv, 10 ff., *ša'ilum* and "ditto *ekli*". The generic ideogram "locust" shows the kind of creature, which is called after a class of interceding priests, and thus corresponds with *μάρτυς* "seer" and a kind of locust or beetle (*Mantis religiosa*, L.). "The Turks and Arabs hold that it prays constantly with its face towards Mecca" (*EB.* xvii, 606).

⁸ *Šapultu*; Jensen, *KB.* vi, 1, 509; GŖS.KUD (*SAI.* 332) = *iš-šu ša-pu-lu*, probably "dry wood". E. "trockenen Speichel".

green . . . , mustard, *asa foetida*,¹ . . . oil therein thou shalt pour . . . set [under] the stars . . .

No. 69. *AM.* 24, 1 (Rm. ii, 143).

1. If ditto . . . pig-fat(?), fir-turpentine . . . in wheat-flour in beer-yeast² in a cup as a com[pound thou shalt mix and apply].

3. If a man's mouth hurts him, it being twisted³ to the right, so that he [can]not speak, his speech he cannot control(?)⁴ for six days thou shalt make his diagnosis,⁵ on the seventh . . . "doves' dung"⁶ wax, fat of *opopanax which contains oil . . . thou shalt knead(?); fat of perfume of cat's(?) dung (civet?)⁷ . . . his eye(?) and his mouth . . . one(?) day, two(?) days, the physician . . .

9. [If a man's mouth hurts him], it being twisted [to the left], so that he [cannot] speak . . . "small palm", . . . gum of *Aleppo pine . . . his mouth . . .

No. 70. *AM.* 24, 5 (K. 6520).

2. . . . his saliva⁸ . . .

¹ The fresh leaves of *Conium maculatum*, L., allay cough (*P.* 437), *asa foetida* is expectorant (*P.* 196), and mustard sialagogue (*P.* 1079).

² *Šuršummu*, about 17 times in *AM.*, commonly *ext.* (and without evidence of internal use). It is of beer, more rarely of "beer and strong beer" (76, 5, 8), and "old beer" (53, 3, 3); its use is as a medium for kneading drugs for a poultice. It is applied for a blow (*mišilti* *re*, 76, 5, 8); to keep away *kurari* (itch, *PRSM.* 1924, 10) (5, 5, 2); for eyes, to knead *lolium* (12, 8, 8); stomachic, probably *ext.* (61, 2, 12); for feet not walking (to knead licorice, **Anacyclus pyrethrum*, and gazelle-dung, 68, 1 *r.* 14); for sickness on body (with wheat-flour, 44, 1, ii, 20); various, 24, 1, 2; 29, 5, 4; 37, 7, 2; 42, 3, 11; 52, 7, 12; 72, 2, 2. Interesting is the pathological comparison "if a man's urine is like *šuršummi šikari*" (66, 7, 4; *KAR.* 193, 13). "Yeast" was suggested by Kūchler, 102, probably correctly. It is "a substance which is deposited in an insoluble state during the fermentation of wine, beer, and vegetable juices" (*PC.* xxvii, 651). It is insoluble in alcohol, and practically insoluble in water, and when exposed to moderate heat loses its liquid portion; it is antiseptic and stimulating (*P.* 1236). Its pathological comparison to urine in *AM.* is either the acid fermentation of urine (Quain, *Dict. of Med.*, ii, 1712), or some turbidity (ib. 1711) not easy to identify. Owing to the presence of *r* and *m* in the root *r š m*, we must probably see its cognate in שָׁמֵר, *Pi.* "to remove the dregs (yeast) from wine", שָׁמֵר "lees, yeast". The other medical product from wine, purified cream of tartar, from cream of tartar or argol, deposited during vinous fermentation (*P.* 966) is impossible, owing to its use internally, not externally.

³ *Kuppul* more probably שֶׁסֶס *devolvit*, *Etpa. convolutus est.* than שֶׁסֶס *vinctus*, or שֶׁסֶס *vinctus*.

⁴ *La ur-ri* (?), or perhaps *tu-šar-ri*.

⁵ *MAŠ.MAŠ.su*, probably *pirsat-su*.

⁶ *AH.* 76.

⁷ *AH.* 87.

⁸ *Illatu*. The Ebeling-Unger translation "Kraft" in the medical text *Archiv. f. Keilschr.* i, 39, is probably incorrect. This text gives in l. 7 a receipt for excess of saliva (*ru'atu*), which with the equations *ru'tu*, *hahhu*, and *illatu* for *uḫ* (Br. 8122), makes it clear that *illatu* is one of the secretions of the mouth. In *AM.* it is used thus: "If while a man talks his *illatu* comes,

3. [If ditto, his mouth] thou shalt cleanse, rose-water in [his] no[stils] thou shalt put] . . . gum of *galbanum, tops (juice) of *Vitex agnus castus* . . . thou shalt pound (and) strain, mix in fat, spread on vellum, [bind on and he shall recover].

6. [If ditto], his mouth thou shalt cleanse, water of *Vitex agnus castus* in his nostr[ils] thou shalt put] . . . , pine-turpentine, fir-turpentine, gum of *Aleppo pine, *Nerium odorum*(?), . . . tops (juice) of tamarisk, tops (juice) of *Crataegus azarolus*(?) together thou shalt pound (and) strain, mix in fat, [spread] on vellum, [bind on and he shall recover].

9. [If ditto], his mouth thou shalt cleanse, tops (juice) of licorice, tops (juice) of *Nerium oleander*(?), tops (juice) of apple, in water thou shalt boil, wash [it]: . . . fir-turpentine, wheat-flour, "doves' dung," gazelle-dung . . . mix in fat, spread on vellum, bind on and he shall recover.

12. [If ditto, his mouth] thou shalt cleanse, in water of *Vitex agnus castus* wash it, pine-turpentine, *Nerium odorum*(?), gum of *galbanum, [ashes?]

he spits *uḡ-su* (= *illat-su* or *ru'ut-su*) in the man's face" (29, 5, 12, cf. 2, 4, 8); (b) "If while a man talks his *illatu* comes" (31, 4, 21); (c) "If a man's *illatu* comes copiously into his mouth and is not stayed" (31, 4, 18), very similar to ib. 11 "If *ru'tu* (saliva) comes copiously into a man's mouth", ib. 14 "If *ru'tu* in a man's mouth is not stayed, that man is bewitched". In (c) for the first the remedy is a compound of tamarisk (gallic acid, astringent, *P.* 551, to lessen discharge from mucous membranes), *galbanum (similar to the expectorant *asa foetida*, but less energetic, *P.* 548), fir and pine-turpentine (expectorant, *P.* 1199); for the second, a compound of fir-turpentine (expectorant), "seed" of tamarisk (astringent) tragacanth (? or savin?), *mint (stomachic, and covering taste of nauseous medicines, *P.* 764), *asa foetida* (expectorant, *P.* 196), hellebore ("in doses short of any dangerous or violent effect, white hellebore exercises a peculiar action on the secreting organs," *PC.* xxvi, 252), stone of *annuḡara* (unidentified), etc. This latter is paralleled by *Archiv. f. Keils.* 7, *Šumma MULU ru'atu-su rabiš illaku vī-ma la ipparasu* "If a man's saliva comes copiously and is not stayed", the remedy being *Salicornia*-alkali, mustard, *asa foetida*, hellebore, and *annuḡara*. L. 1 ff. of the same text "If a man's *illatu* comes, etc., for his recovery and to stop his *illatu*" (*ana balati-su u il-la-ti-šu pa-[ra-si]*), for which 15 še of lupins, hellebore, tragacanth(?) (or savin?), licorice root, **Chrysanthemum segetum* are to be compounded. It seems therefore clear that *ru'tu* must be the same as or closely allied to *illatu* in meaning, and that "saliva" is almost certainly correct for this latter.

Of the other equivalents for *uḡ*, *rupuštu* = 𐎶𐎶𐎶 "mud, slime" (*MA.* 978, quoting authorities; Kū. "Auswurf"). [*Šumma N*]A *riš libbi-šu rupulta iši vī-ši riš libbi-šu uṣarab-šu* "If a man's epigastrium holds heartburn, his epigastrium burning him" (48, 2, 1). *Rupuštu* is, I presume, the acid eructation usual in such stomachic trouble; "Heartburn is a hot or scalding sensation . . . frequently accompanied by eructations of a very acid character" (Quain, *Dict. of Med.* i, 633). I prefer *ṣarabu*, sufficiently well attested for "burn" (*MA.* 892; Del., *HWB.* 573) and paralleled by *iḥamat-su* (*AM.* 45, 6, 5 and 6), to *zarabu* "press" (*E.* xiii, 3), but the latter is possible. Cf. also "*rupuštu* in his mouth" (24, 3, 10; and cf. Kū. ii, ii, 39, 44; iv, 34).

The other equivalents for *uḡ* must have similar meanings. *Uḡḡu*, probably similar to 𐎶𐎶𐎶 "to cough", *ḥaḡḡu* "phlegm" (*Auswurf*, Holma, 9); *ḥurḡummatu*, also an equivalent for *u* (*Br.* 8684); and *kušū*.

of an oven together thou shalt pound (and) strain, mix in fat, spread on vellum, bind on and he shall recover.

14. [If . . .] hurts him,¹ in his mouth flour-dust² of millet . . . dried [roses ?] he shall spread,³ "[human] skull" . . . ; he shall lick the upper stone of a *Lolium*-mill⁴ [and he shall recover].

No. 71. *AM.* 28, 2 (K. 3295).

1. [If a man is attacked by] . . . and he has mouth-trouble, . . . his tooth (mouth) troubling, his saliva flowing unceasingly, . . . and blood exuding :⁵

4. (Mutilated.)⁶

No. 72. *AM.* 29, 1 (K. 8777) + 89, 3 (K. 10429 + 11677), now joined to K. 2175, *CT.* xxiii.

No. 73. *AM.* 29, 5 (K. 3461).

4. If ditto, sediment of the river, yeast of beer, . . . *Lolium*, roses, *ammi, seed of *kan*[*kadu*](?), pine-turpentine, fir-turpentine, in equal portions thou shalt mix in water, dry in the sun : beat up again, boil in oil in a pan, beating it up ; beat up again in fat, touch with sweet oil, spread on vellum, bind all his flesh : thou shalt bray ***Calendula*, lupin, *corn-marigold, mix in oil, leave out under the stars, let him drink without a meal.

12. If a man's saliva comes when he is talking (and) he ejects his spittle into a man's face, his teeth ache, his mouth hurting(?)⁷ him, the eructation of . . . , that man's trouble⁸ (is) . . . ; myrtle, suadu, seed of . . . , seed of caper, seed of *Lycium*, . . . , alum, . . . tamarisk-seed . . .

No. 74. *AM.* 30, 2 (S. 1524).⁹

2. . . . : If ditto, thou shalt slice a leek, [rub it on the root of his tooth, and he shall recover].¹⁰

¹ [*It-t*]a-na-ka-la-šu.

² Cf. *AM.* 30, 8, 5.

³ *Isarra*?, see No. 65, i, 5.

⁴ *TAK.NA sahlī ilik*, also 36, 2, 9 ; *ina TAK.NA RAT*, 91, 5, 4 ; *ina TAK.NA sahlī RAT*, 40, 1, 63 ; *ina NA sahlī RAT*, 14, 8, 7. *TAK.NA* = *abnu elā* "the upper (mill)-stone", and *TAK.NA sahlī šar* = *elit urši* (cf. *kalab urši*, ii R. 6, a-b, 18), Br. 1584. *Uršu* = *mazuktu* (*HWB.* 137), and *elit urši* = *amitti* ,, (ib.) ; *mazuktu* = "a mortar" (*E.* xiii, 6, n. 4), so that *TAK.NA* will be "the upper stone", especially of a mortar used in grinding *Lolium*, doubtless smaller than the usual bread-mill, since drugs are to be ground in it (cf. the manna of Num. xi, 8). Cf. *akur-ši*, *CT.* xxiii, 50, 17. *Ilik*, 𐎠𐎢𐎫 "lick".

⁵ *Ihila*, probably same root as *hīlu* "gum" (𐎠𐎢𐎫 "dance", "writhe", i.e. "roll" ?).

⁶ For "the Temple of Marduk" cf. 76, 5, 5, 6 ; 93, 1, 8 ; 105, 1, 4. Cleansing the teeth is part of the receipt.

⁷ *Ihtanaliḫ-šu*.

⁸ *Nullatī* (v. Del., *HWB.* 454), 𐎠𐎢𐎫 *vezavit*.

⁹ *AM.* 29, 13 (K. 3236) may be the tablet preceding Ebeling-Unger, *Arch. f. Keils.*, i, 36.

¹⁰ See *AM.* 36, 2, 11. *Eḫir*, 𐎠𐎢𐎫 "root". Cf. *SM.* ii, 189, 667, garlic applied to hollow teeth.

3. [If ditto] . . . *ammi, seed of *Eruca*,¹ salt, alkali . . . thou shalt bray, mix in refined (?)² oil bind on.

5. [If ditto] . . . nettle-seed thou shalt bray, in oil thou shalt mix, anoint.

6. [If ditto] . . . [the fat ?] of a lion,³ the liquid⁴ of a cricket,⁵ the gall of a snake, . . . , the blood of an *anduhallatu*⁶ lizard in oil thou shalt mix, anoint.

7. [If ditto] . . . *Lolium* in oil thou shalt mix, anoint.

8. . . . and his mouth is puckered,⁷ its name is *ziḫtu*⁸ : . . . and his mouth is broken, its name is *ziḫtu* : . . . hurts him, its name is *ziḫtu* : If the affected spot is dark(?) (and) small(?) and hurts him, its name is *ziḫtu*. Thou shalt bray . . . pine-turpentine, mix in *kurunnu*-beer, bind on him and he shall recover.

13. . . . in the suet of a ram's kidney thou shalt mix, spread on vellum, bind on : . . . wax in fat thou shalt mix, bind on.

15. . . . their mark . . .

No. 75. *AM.* 30, 3 (K. 7656) + 18, 11 (K. 9144) + 26, 10 (K. 16448).

Col. ii.

2. *Šumma ditto šar* (?) . . .

3. *tur-di ka* . . . *iš tu* . . .

4. *ba-lit-tu ni* (?) . . . *iḏḫu šu* . . .

¹ Used here for teeth on account of its "hot" seeds.

² *Kirrani*, كَرَر "refine".

³ "Lion fat" is a name for opium, *AH.* 46.

⁴ *Ta-lil* (?) ܬܐܠܝܠ "dew", ܠܝܠܐ humor, ܠܝܠ "milk, blood". But *lil* (?) may be *ta* or *um*.

⁵ *Lalara* (*MA.* 482, "cricket?" for *lallartu*) must be *Gryllus domesticus*, L., from the shrill repetitive noise indicated by *lalaru*, like the ululation of the professional mourner (cf. the rapid "'Ali, 'Ali, 'Ali" of the women at Muharram).

⁶ *Anduhallatu* (cf. Weidner, *RA.* 1914, 119), from *SAI.* 525, must be a kind of lizard. The sign *gi* in 525 must surely be *zi* (cf. *AM.* 61, 5, 10, and *SAI.* 526, *EME.MIŠ.GIŠ.GI* = *šuraru ša igari*, the latter part of which must be *GIŠ.ZI*, cf. *Br.* 5709, *GIŠ.ZI* = *igaru*). The group *EME.MIŠ* must undoubtedly refer to the way in which the lizard uses its tongue, as anyone who has seen the agile "lizards of the wall" in Basrah will remember. It must surely be divided *andu* (= *amtu*, as in late Babylonian = "handmaid") *hallatu*, i.e. "creeping handmaid."

⁷ *Hundud*, doubtless with a "resolved" *d* (like *pungulu*), from ܚܕܕ "to be wrinkled". The cure indicates that it does not mean a "hare-lip".

⁸ *Ziḫtu*, properly a sting or point.

5. If ditto, *mušdim* [*gurinna*], its fat . . . , *haematites*, fourteen times

7. *Šumma* ditto *tam* (?) *šil* (?) *gas si* (?) . . . *dī im a-šar takī-* . . .

8. *bu-za-bur-ru kur-ba-* . . . *eli pî-šu tašakan (an)* . . .

9. *kima mê ša ana eli pî-šu* . . . *ut-ta* . . . *ši* . . .

10. If ditto, thou shalt (?) . . .¹ male mandrake-root, its juice thou shalt put on his aching tooth. If ditto, thou shalt pound a *humbibitu*,² roll (it) up in wool, sprinkle with oil put (it) into the ear (on the side) of the aching tooth.³ If ditto, thou shalt bray *Nigella*, put it on his tooth. If ditto, thou shalt bray hellebore,⁴ anoint his tooth therewith.

14. . . . created Anu, Anu the host of heaven, Anu the host of earth : the earth created the W[orm] : . . . the foetor, which hath increased the foetor, hath seized him as a lion seizeth the throat of a cow (?), [as a jackal] seizeth a steer, [as a . . . tearer (?)] flesh, so hath the Worm established her seat amid the teeth ; [as one who is distant] forgetteth his city-street, [as a dead man passeth not the gate of life, as an untimely birth sucketh not] the breast of its mother . . . [*ana šip*]-*ti-šu* . . .⁵

No. 76. *AM.* 30, 4 (K. 13801).

2. . . . thou shalt bray . . . , put on his tooth : thou shalt bray . . . , put on his tooth

5. . . . put on his tooth : . . . put on his tooth.

No. 77. *AM.* 30, 6 (K. 2510).

Obv. 1. (*End of Sumerian charm.*) . . . like water from a well . . . : neither drug nor water entereth : . . . Marduk hath seen : "What I" ; "Go, my son,"⁶ . . . and take thyme,⁷ put it . . . , put it on the tooth of the man, son of his god ; . . . (?) he shall recover : as he goeth, the . . . shall go forth.

¹ *Ta* (?) *-na-ad-da*.

² Fossey, *Babyloniaca*, v, 1, 8-9, 73, "if a woman bear a *humbabitam*." *Hum-bi-bit-tum*, Weidner, *RA.* 1914, 119.

³ Cf. *SM.* ii, 189 : "pour into the ear on the side of the face which is affected."

⁴ *Nigella* for teeth, *SM.* ii, 189 ; hellebore, *ib.* 185.

⁵ Cf. *AM.* 36, 2, iii ; *KAR.* 181 r. 11 ; *CT.* xxiii, 10, 16.

⁶ For this abbreviated incident see my *Semitic Magic*, xlvii.

⁷ In *AH.* 195 I mentioned that we did not yet know the Sumerian for this plant ; and the Sumerian charm uses the Assyrian word, as though the Assyrian form alone was known. For oil of thyme on a decayed tooth cf. *ib.* 195. I cannot agree with Ebeling's later view (doubtless on the strength of *HAR* = *hašû*, *SAI.* 6418) that "*HAR.HAR* = *hašû* "thyme" (see *Arch. f. Gesch.* xiv, 26, 17) ; (see *AH.* 64 = mustard).

7. . . . thou shalt perform the charm, in his mouth he shall mix,¹ and drink in beer, and he shall recover.

Rev. 1. . . . may his tooth be freed, . . . of Eridu . . . may his knot be loosed!

3. . . . [the charm] seven times thou shalt repeat, in his mouth he shall mix,¹ and he shall recover.

4. [If a man's] . . . binds him and creeps(?)² . . . to its front, not the side(?) . . .

7. . . . *asa foetida*³ thou shalt take, thereon perform the charm . . .

No. 78. *AM.* 30, 13 (81-2-4, 418).

2. . . . myrrh . . . , *asa foetida*,³ . . . *asa foetida* on his tooth thou shalt spread . . .

5. If ditto, sweet *usa*-beer . . .

(For ll. 6-8 see No. 65, i, 7.)

No. 79. *AM.* 31, 4 (K. 2417).

Obverse. 2. . . . *asa foetida* . . .

3. . . . thereon thou shalt put, in . . .


4. . . . *asa foetida* thou shalt bray, put thereon . . .

5. . . . sulphur(?) thou shalt bray . . .

6. [If] sorcery attacks [a man], thou shalt remove the end and root⁴ of lupins, bray their middle part . . .


7. [If a man's] . . . is sick, and his sleep is kept away thereby,⁵ "salt of Akkad" . . . either [in beer] or in oil thou shalt put, set (it) under the stars . . .

9. (*Dup. of 44, 5, 6.*) [If a man's . . . is sick] and his sleep is kept away thereby, fifteen rubbed(?)⁶ grains of *Lycium*, fifteen rubbed(?) grains of . . . together thou shalt rub⁷ in half a shekel of ox-fat, apply by his anus [and he shall recover].

¹ *Umanzag*  "mix".

² *Išpapa*; *šapāpu* = *alāku* (*MA.* 1087); cf. .

³ Cf. *SM.* ii, 189.

⁴ *Pā u išdu*, cf. .

⁵ *Šitta-šu etanabbal*, cf. next par. and 57, 5 r. 1.

⁶ *Sikti*, see No. 33, 3, n. The correct reading is "15".

⁷ *Tusamah*; various drugs thou shalt bray, with fat *tusamah* (*KAR.* 195 r. 34); *lu gab dišpi u* ²*gIL tusamah* (*Kū.* ii, ii, 43); . . . *ZIZ.A.AN tusamah* (*AM.* 72, 2 r. 9); cf. *CT.* xxiii, 50, 14. *Kū.* "verreiben?"

11. [If] the saliva in a [man]'s mouth comes too freely,¹ [thou shalt bray] fir-turpentine, tamarisk-"seed" (=gall), savin(?) (or tragacanth(?)), . . . , *mint, *asa foetida*, . . . , hellebore, stone of *annuhara*, stone of . . . in the night before the Goat-star² thou shalt set . . . without a meal in beer [he shall drink, and he shall recover].

14. If the saliva in a man's mouth does not cease to flow, that man has been bewitched: for [his] recovery, thou shalt bray together . . . *eligulla*, savin(?) (or tragacanth(?)), [he shall drink] in *kurunnu*-beer, [and he shall recover].

16. If the saliva in a man's mouth does not cease to flow, that man has been bewitched: for his recovery thou shalt bray together³ . . . mustard, **oak-galls, licorice-root, *liquidambar, [he shall drink, and he shall recover].

18. If a man's saliva comes too freely in his mouth, without ceasing . . . tamarisk (-galls), *galbanum, fir-turpentine, pine-turpentine together thou shalt bray, [he shall drink and recover].

20. To make his saliva flow,⁴ spurge like . . .

21. If a man's saliva comes while he is talking, myrtle(?) . . . , *Lycium*, *mint . . .

Rev. 1. Earth and Hell its figure, from Hell . . . and his muscles; his semen which on close-stool(?)⁵ . . . (or) in bed has passed. Charm. This charm thou shalt recite three times over . . .

4. Cinnabar, oxide of iron, *lapis lazuli*, *alabaster⁶ . . . thou shalt thread, on his neck hang.

6. . . . *borax in beer . . .

7. . . . *asa foetida*, **Arnoglosson*, *asa (dulcis?)*, . . . male mandrake: these seven drugs thou shalt bray together, [he shall drink, and he shall recover].

¹ See Ebeling-Unger, *Arch. f. Keils.* i, 36, 7.

² Cf. Landsberger, *Arch. f. Keils.* i, 77.

³ *Itti ahamis*.

⁴ *Ana illatu-su šuluka(ka)*. For *kasi amhara* = *Euphorbia helioscopia*, L., see AH. 37.

⁵ *KU mithurti*, surely the same as *GIŠ.GU.ZA.NIGIN.NA* = *kussi mithurti*, Br. 11160. If *mithurti*, through its meaning "agreement, harmony", can = "ease" (i.e. lieu d'aisance), then there is no difficulty for this explanation, which the parallelism of "bed" seems to demand. The Assyrian latrine even in a temple (as I found in digging out the Temple of Nabû at Nineveh for the British Museum in 1904-5) is the same as the modern Oriental equivalent, a slit in the floor over a drain. Cf. E.KU.DAM (Holma, 68, "w.c. für Damen").

⁶ These must surely refer to colours, vermilion, black, blue, white, of beads.

9. . . . thou shalt knead in . . . beer ("old break"), [spread] on vellum, [apply, and he shall recover].

10.

11. . . . his semen, intentionally or not,¹ floweth . . . tops (juice) of tamarisk (= gall), *Crataegus azarolus* (?), *tulal*,² ***Calendula*, *corn-marigold . . .

13. (*Fragmentary incantation.*)

¹ *Ina piḫi la piḫi*, which occurs as *ina piḫam la piḫam*, *CT.* xxiii, 13, 18, followed by *iparrud* (glossed *izarrud*, probably more correct). *Iparrud* is not satisfactory; *izarrud* may be 𐎶𐎵 *suffocavit*. I cannot agree with E. (xiii, 143) "er unregelmässig (?) Frost hat". Cf. *ki-i pi-i-gi* (Scheil, *Rec. des Lois Assy.*, 26, iii, 30).

² It has certain similarities with *Atropa Belladonna*, L. Cf. *AH.* 203 with *AH.* 105.

** (a) "Mercury" used in the above translations must still be considered doubtful. (b) *LA* has the certain meaning "ashes". (c) The exact translation for "salt of Akkad" is doubtful.

Section of the History of Medicine.

President—Dr. J. D. ROLLESTON.

Voltaire and Medicine.

By J. D. ROLLESTON, M.D. (President).

PART II.

AT the last meeting¹ I dealt with Voltaire's own medical history, his relations with individual medical men and his appreciation of the medical profession as a whole. I shall now give some account of his other relations to medicine, namely his allusions to anatomy and physiology, his advocacy of inoculation, his interest in the history and ravages of syphilis, his attention to other matters relating to public health, his acquaintance with medical jurisprudence and particularly his sceptical attitude towards historical cases of poisoning, and his description of various diseases of social importance, such as convulsive hysteria at the tombs of saints and ecclesiastics, alcoholism and the king's evil.

ANATOMY AND PHYSIOLOGY.

Several passages, such as his description of the structure of the eye (*Eléments de la Philosophie de Newton*, Chap. V), ear (*Tout en Dieu*), lacrymal gland (*Dictionnaire Philosophique*, Art. Larmes), and muscles of expression (*ibid.*, Art. Rire, *Questions sur les miracles*, Lettre XIV), show that Voltaire had paid some attention to anatomy. He commences his article on Man in the *Dictionnaire Philosophique* by saying that in order to learn the physical aspects of the human race, one should read works of anatomy, the article in the *Dictionnaire Encyclopédique* by M. Venel, or, rather, follow a course of anatomy. In his article on Anatomy in the *Dictionnaire Philosophique* he remarks that:—

"Ancient anatomy bears to modern anatomy the same relation that the rough geographical charts of the sixteenth century, which merely represented the principal places—and even those inaccurately—bore to the topographical maps of to-day, in which even the smallest thicket is marked."

Voltaire, however, fully realized that much was yet to be learnt in human anatomy:—

"Although," he says (*De l'Âme*, I), "there is not at the present time a doctor in Rome or Athens, who does not know more anatomy than Hippocrates, no one has ever been able to obtain knowledge of the first principle from which we derive life, feeling and thought."

In the chapter entitled "Incertitudes en Anatomie" in the essay *Des Singularités de la Nature*, he exclaims:—

"In spite of all the help that the microscope has given anatomy, and in spite of the great discoveries of so many skillful surgeons and physicians, what interminable discussions have arisen, and in what uncertainty we still remain."

The following remarkable passage showing the necessity of a knowledge of Greek for the proper understanding of anatomical terms may here be quoted:—

¹ *Proceedings*, 1925, xix (Sect. of Hist. of Med.), pp. 17-28

"What term in art is not derived from this admirable language? There is hardly a muscle, a vein, a ligament in the body, a disease or a remedy which is not Greek. Take two young persons, one of whom knows this language, while the other does not. Let neither have the slightest inkling of anatomy, and tell them that one man is ill with diabetes, that another will require paracentesis, and that another has an ankylosis or bubonocoele. He who knows Greek will at once grasp your meaning, because he sees of what the words are composed, while the other will understand nothing at all" (*Conseils à un journaliste—Sur les langues*).

In the *Essai sur les Mœurs* (Chap. CLVIII) he relates how the science of anatomy in Persia perished with all the others, but was resuscitated in Europe at the beginning of the sixteenth century by the discoveries of Vesalius and the genius of Fernel. On more than one occasion Voltaire's knowledge of anatomy served a literary purpose. In the description of the wounds inflicted by Dunois, the companion of Joan of Arc, the use of anatomical terms has a burlesque effect:—

"Il perce à l'un le sternum et le bras,
Il atteint l'autre à l'os qu'on nomme atlas,
Qui voit tomber son nez et sa mâchoire,
Qui son oreille, et qui son humerus,
Dunois le joint, l'atteint à l'os pubis,
Le fer sanglant lui sort par le coccyx."

(*La Pucelle*, VII, 283.)

In this connexion mention may be made of the celebrated "nerf de Voltaire," which is an imaginary nerve running from the brain to the organs of generation via the eyes, lips and heart (*Dictionnaire Philosophique*, Art. Baiser; *Dialogue entre Lucrèce et Poseidonius*; *Les Adorateurs*).

It is probable that this conception was not a mere *jeu d'esprit*, in view of the fact that the rôle of the nerves in the economy was still in the realm of nebulous hypotheses. It must be remembered that it was not until the time of Charles Bell (1811) and Magendie (1812) that the functions of the nerves were fully understood. Jean Paul Marat in his work *De l'Homme* (1775) suggested the existence of a nervous fluid (*suc des nerfs*) as the connecting link between the body and the soul, but had incurred a scathing review from Voltaire (Articles extraits du *Journal de Politique et de Littérature*), not only for this hypothesis but also for his attack on Helvétius, who in his book *De l'Esprit* had declared that a knowledge of science was unnecessary for a philosopher.

Although physiology was still in its infancy during the eighteenth century, Voltaire appears to have been well abreast of the knowledge of the time. In his article on Anatomy in the *Dictionnaire Philosophique*, which is really more concerned with physiology than anatomy, as well as in the essay entitled *Les Adorateurs*, he alludes to the uncertainties current in connexion with circulation, digestion, generation and muscular tonicity. Elsewhere he gives some account of the physiology of digestion (*Dictionnaire Philosophique*, Art. Déjection) and Vision (*Eléments de la Philosophie de Newton*, Chap. V), and alludes to the pioneer work of Borelli, Keil and Jurin in cardiac physiology (*Dictionnaire Philosophique*, Art. Anatomie; *Singularités de la Nature*, Chap. XXXV).

Commenting on the statement of Descartes that—

"Envy propels the yellow bile that comes from the lower part of the liver and the black bile that comes from the spleen and passes from the heart by the arteries, &c.,"

Voltaire sarcastically remarks that:—

"As no kind of bile is formed in the spleen, Descartes should not make us envy him his physics." (*Dictionnaire Philosophique*, Art. Envie.)

In another passage (*ibid.*, Art. Cartésianisme) he points out several errors of Descartes in connexion with digestion and circulation.

The casuist Sanchez (*Les questions de Zapata* 50) and the philosopher Maupertuis (*Extrait de la Bibliothèque raisonnée*) also incur considerable ridicule for their extraordinary views on generation and embryology.

Like his contemporary Casanova,¹ Voltaire seems to have had a firm belief in the doctrine of maternal impressions, as is seen by the following passage from the *Dictionnaire Philosophique* (Art. Influence):—

"I believe that the violent affections of the pregnant woman have a remarkable effect upon the embryo in her womb, and I think that I shall always believe it. My reason is that I have seen it. This influence has been denied. It has been asked 'How can the affections of a mother influence the limbs of a fetus?' I do not know, but I have seen it."

As an example of maternal impressions he quotes the case of James I, whose tremors he attributes to the effect which the spectacle of Rizzio's assassination had upon Mary Stuart (*Essai sur les Mœurs*, Chap. CLXIX).

INOCULATION.

Throughout his life Voltaire was an ardent supporter of inoculation against small-pox. The eleventh letter of the *Lettres Philosophiques*, which was first published in 1727, is devoted to the history and description of the method. In this letter, speaking of Lady Wortley Montagu, he remarks that if the French Ambassador's wife had brought the secret of inoculation from Constantinople to Paris she would have rendered an eternal service to the nation.

"Not only would the members of several noble houses such as the Duke of Villequier, the Prince of Soubise, and the grandfather of Louis XV have escaped the disease, but 20,000 who had died of smallpox in Paris during 1723 would still be alive."²

In a letter to D'Argental (October 3, 1753), he alludes to the Bishop of Worcester preaching in London in 1752 before Parliament in favour of inoculation and showing that it saved the lives of 2,000 persons in the capital every year. About the same time he tells the Comtesse de Lutzelbourg (October 24, 1753) that she will never hear of any lady dying of small-pox in London, and that if he had a son, he would have him inoculated before teaching him his catechism.

The prohibition of inoculation by an edict of the French Parliament of June 8, 1763, as the result of an address by the Attorney-General, Omer Joly de Fleury, attributed to the action of Bouvart, an enemy of Tronchin,³ provoked bitter protests from Voltaire. Writing to Damilaville (June, 1763) he says:—

"The absurdity of this new decree was the only one left for my dear country. . . . We are the laughing stock of Europe."

And in a letter to D'Argental (June 18, 1763) he suggests that the decree was due to a desire to bring persons to Geneva where Tronchin enjoyed such a great vogue as an inoculator. He also tells Richelieu (June 12, 1763) that everyone will come to Geneva to be inoculated, and the town will have to be enlarged. In a previous letter to the same correspondent (May 1, 1755), he had said that the method was as popular and successful in Geneva as it had been in England.

The following extract may be quoted from the leaflet entitled "Omer de Fleury étant entré ont dit," which is a parody of that magistrate's address to the French Parliament on behalf of the prohibition of inoculation:—

¹ *Janus*, 1917, xxii, p. 216.

² Lanson in his edition of the *Lettres Philosophiques* has shown that this figure is inaccurate, as according to the *Encyclopédie* (Art. Inoculation) the annual mortality in Paris from all causes was reckoned at 20,000.

Delaunay, *loc. cit.*, p. 293.

"Since inoculation, gentlemen, is successful in all the neighbouring countries which have tried it and has saved the lives of foreigners who can reason, it is right that you should forbid the practice, since it has not been registered, and for that end you will avail yourselves of the decisions of the Sorbonne which will tell you that St. Augustine had no knowledge of inoculation . . . We hope that you will decree the penalty of death which the Faculties of Medicine have sometimes decreed in less important cases against the children of our princes who have been inoculated without your permission."

From the correspondence with Catherine the Great, who had introduced inoculation into Russia under the influence of Voltaire, we learn how popular the practice had become in that country. In a letter dated December 6-17, 1768, Catherine tells him that "everyone here wishes to be inoculated and within a month more have been inoculated than at Vienna in eight months." In reply (February 26, 1769), Voltaire congratulates her on having been inoculated herself "with less fuss than a man makes on having an enema."

In the essay entitled *De la Mort de Louis XV*, published in 1774, that is, four years before his death, Voltaire instances the good examples set by the Duke of Orleans, the Duke of Parma, and the Kings of Denmark and Sweden, who had had themselves and their children inoculated.

"There is no operation," he says, "which is so easily performed. It is less dangerous than bleeding, in which there is always a risk of pricking a tendon. A nurse or a servant can inoculate a child as safely as a doctor of medicine, provided the subject is in good health, and for the sum of a crown one can save the lives of all the little children in a village."

Voltaire never seems to have realized the principal objection to inoculation which was one of the reasons of its prohibition by the French Parliament, namely, the creation of a fresh focus of infection, though he admits (*Lettre à Madame du Deffand*, October 16, 1765) that in one out of 20,000 cases natural small-pox may occur, and even be fatal (*Dictionnaire Philosophique*, Art. Tonnerre).

It is noteworthy that Tronchin in his article on inoculation in the *Encyclopédie* made light of the objection and declared that the supposed danger of contagion from artificial small-pox was imaginary.

SYPHILIS.

Syphilis is undoubtedly the disease to which most references are made in Voltaire's works, especially in the *Essai sur les Moeurs* (Chap. CXXV, CXLV), *Dictionnaire Philosophique* (Arts. Amour, Frivolité, Job, Lèpre et Vérole, Population, Puissance—Toute Puissance), and in the stories *Candide* (Chap. III and IV), *L'homme aux quarante écus* (Chap. XI), *L'histoire de Jenni* (Chap. IX), *Les Oreilles du Comte de Chesterfield* (Chap. VI), *Memnon* and *Lettres d'Amabed* (Lettre XVI). Other allusions will be found in *La Pucelle* (Chart XIII, 326), *Poésies mêlées* XCVII, *Omer de Fleury*, *L'A, B, C* (16e entretien), *Le philosophe ignorant* (§ XXVI), *Il faut prendre un parti* (§ XVI), *Lettre à M. Beccaria*, *Lettre de M. de Voltaire à la noblesse de Gevaudan*, *De la Mort de Louis XV*, and *La Bible enfin expliquée*—Lévitique, Nombres.

In discussing the early history of syphilis, the knowledge of which he had undoubtedly derived from Astruc's treatise, Voltaire bases his belief in its American origin, first on the evidence of a large number of physicians and surgeons of the sixteenth century and secondly on the silence of all the medical writers and poets of antiquity.

"Medical men from the time of Hippocrates," we read in the *Dictionnaire Philosophique* (Art. Lèpre et Vérole), "would never have failed to describe the disease, give it a name and try to discover a cure for it. The poets, who were as spiteful as the medical men were industrious, would have mentioned scalding urine, chancres, buboes, and all the antecedents and conse-

quences of this frightful disease . . . You do not find a single line in Horace, Catullus, Martial or Juvenal which has the least relation to syphilis, whereas they dilate complacently on all the effects of debauchery."

Voltaire fully realized the distinction between leprosy and syphilis, and holds up to derision the erudite Benedictine Dom Calmet, who maintained that syphilis was the most malignant form of leprosy and that Job suffered from it (*Dictionnaire Philosophique*, Art. Job; *La Bible enfin expliquée*—Lévitique).

As a proof of the non-identity of the two diseases, Voltaire mentions the fact that on the appearance of syphilis in Europe the few remaining lepers resented association in hospital with syphilitic patients,

"just as persons in prison for debt or affairs of honour object to mixing with the ordinary prison population." (*Dictionnaire Philosophique*, Art. Lèpre et Vérole.)

Dom Calmet had also tried to find in Juvenal's well-known lines

"sed podice levi
Caeduntur tumidae, medico ridente, mariscae"
(*Sat. II, 12*),

an allusion to syphilis, but as Voltaire shows, this passage merely refers to the mechanical injury caused by sodomy.

Just as leprosy had been the only permanent acquisition from the Crusades (*Dictionnaire Philosophique*, Art. Lèpre et Vérole), syphilis was all the French gained from their invasion of Italy.

"Quand les Français à tête folle
S'en allèrent dans l'Italie
Ils gagnèrent à l'étourdie
Et Gène et Naple et la v——.
Puis ils furent chassés partout,
Et Gène et Naple on leur ôta,
Mais ils ne perdirent pas tout,
Car la v—— leur resta."

(*Poésies mêlées*, XCVII.)

Voltaire's description of the American origin of syphilis is to be found in the following passage of the *Essai sur les Mœurs* (Chap. CXLV).

"Although the discovery of America was at first a considerable benefit to the Spanish, it also brought very great misfortunes upon them. In the first place, Spain was depopulated by the number required for its colonies, and secondly, the universe became infected with a disease which previously had only been known in some parts of the other hemisphere, and especially in the island of Hispaniola. Many of Christopher Columbus's companions were attacked by it and spread the contagion throughout Europe on their return. It is certain that the venom which poisons the source of life was peculiar to America, just as plague and smallpox were the original diseases of South Arabia."

Voltaire then dismisses the view that syphilis was due to cannibalism, as there were no cannibals on the island of Hispaniola where the disease had been known from time immemorial.

A similar description of the American origin of syphilis is given by a surgeon in reply to an inquiry as to the date of its first appearance in Europe (*L'homme aux quarante écus*, Chap. XI).

The originally mild character of the disease to which some of the early writers mentioned by Astruc allude, is emphasized in the *Histoire de Jenni* (Chap. IX), in which the Chaplain Freind declares that it was cured in two days either by guaiacum or turtle broth, and that it was only after its transplantation to Europe that it became such a terrible scourge, as is exemplified in the case of the philosopher

Pangloss (*Candide*, Chap. III and IV) and the two cousins of *L'homme aux quarante écus* (Chap. XI), where the description shows that Voltaire was familiar with the action of syphilis on the skin, hair, larynx, bones, eyes and ears.

The salivation, stomatitis and necrosis of the jaw so frequently associated with mercurial treatment in the eighteenth century are alluded to in several passages, as in the case of Pangloss and the cousins of *L'homme aux quarante écus* already mentioned, and one of the witnesses in the trial of the Comte de Morangiés (*Lettre à M. Beccaria, Précis du procès du Comte de Morangiés, Lettre de M. de Voltaire à la noblesse de Gevaudan*).

"Few weak chests," says the surgeon in *L'homme aux quarante écus* (Chap. XI), "can resist the disease, and fewer still the remedy."

Among the early illustrious victims of the disease mentioned by Voltaire are Leo X (*Histoire de Jenni, Lettre d'Amabed*, XVI), François I, Charles V (*Essai sur les Mœurs*, Chap. CXXV), Henri III, the Duke of Mayenne (*Il faut prendre un parti*, § XVI), and the Bishop and Viceroy of Hungary (*L'homme aux quarante écus*, Chap. XI).

The prevalence of syphilis among the royalty, nobility and high clergy is attributed to the houses of prostitution reserved for their use (*ibid.*). The high incidence of the disease among soldiers is mentioned in *Candide*, *L'homme aux quarante écus* and *Poésies mêlées*, XCVII.

"The disease," says Pangloss (*Candide*, Chap. IV) "has made a marvellous progress among us, and especially in those great armies which decide the destinies of the State; one may affirm that when 30,000 men are fighting against an equal number of troops on the opposite side, there are about 20,000 suffering from the disease in each army."

The spread of syphilis in a small canton after the introduction of troops is described in *L'homme aux quarante écus* (Chap. XI), where we read that

"two lieutenants, the chaplain of the regiment, a corporal and a recruit who had just left a seminary were sufficient to poison twelve villages in less than three months."

The lucrative nature of a venereal practice, of which Casanova¹ has also given a striking example, is illustrated in two passages, one in *Les Oreilles du Comte de Chesterfield* (Chap. VI), where the surgeon Sidrac declares that he owes syphilis the greatest part of his fortune, and the other in *L'homme aux quarante écus*, where another surgeon states that war and syphilis were the sources of his fortune.

In one of the many passages in his works where he was far in advance of his time, Voltaire recommends that a league of nations should be formed for combating syphilis.

"Are there no means," *L'homme aux quarante écus* exclaims, "of extirpating a contagion which devastates Europe?"

To which the surgeon replies:—

"There can only be one way. All the princes of Europe should form a league as in the time of Godfrey of Bouillon. Certainly a crusade against syphilis would be much more reasonable than those wretched crusades against Saladin, Maliksala and the Albigenses. It would be much better to learn how to repel the common foe of the human race than to be continually occupied in watching for the favourable moment to devastate the earth and cover the land with corpses in order to deprive one's neighbour of two or three towns or a few villages."

It was not until over 150 years later that Voltaire's proposal was realized by the foundation at Paris on January 27, 1923, of the "Union internationale contre le péril vénérien," to which at the present time thirty-three nations belong.

The confusion between gonorrhœa and syphilis, which, prior to the middle of the sixteenth century, had been regarded as distinct diseases, but were subsequently confounded until the time of Ricord, "the Voltaire of pelvic literature," is illustrated in the few passages in which Voltaire alludes to gonorrhœa usually under the popular term "Chaudepisse," just as he invariably uses the word "vérole" to designate syphilis.

In one passage (*La Bible enfin expliquée—Nombres*), where he uses the term "gonorrhœa" he makes a distinction between a non-contagious disease which would now be called spermatorrhœa, and a virulent form which, he says, was not known in France before the end of the fifteenth century, is well known to be contagious through sexual intercourse, and if neglected, is infallibly followed by syphilis.

PUBLIC HEALTH.

Voltaire's interest in public health is shown not only by his desire to stamp out certain contagious diseases, such as small-pox and syphilis, but also by his allusions to other epidemic diseases, his condemnation of the insanitary condition of the Paris hospitals, the abuses connected with the administration of military hospitals, the crowded state of the Paris cemeteries, and the practice of burial in churches, as well as by his proposal to found maternity hospitals for unmarried women.

In several of his historical works he recognized the importance of epidemic diseases, although the nature of the outbreak is not always stated. It is probable, however, that bubonic plague, typhus, relapsing fever, malaria and influenza, were the principal diseases in question. In the *Essai sur les Mœurs* (Chap. LXXIX) it is expressly stated that an epidemic of contagious dysentery caused the death of three-quarters of the army of Henry V which had invaded France.

In the *Histoire de la Russie sous Pierre Le Grand* (Chap. XVI) we read that

"Charles XII could not make rapid progress in his movement to the east by Lithuania during the winter in marshy countries infected with contagious diseases which as the result of poverty and famine had spread from Warsaw to Minsk."

In the same history (Chap. XIII) we are told that during the building of St. Petersburg "epidemic disease carried off a prodigious number of workmen."

Apart from inoculation several allusions are to be found in Voltaire's writings to small-pox, from which, as I have said, he suffered himself. In a letter to Paulet, the author of several works on the disease, he writes on April 22, 1768:—

"I do not know which of these two young ladies (small-pox and syphilis) has done the greatest harm to the human race,"

and in the *Dictionnaire Philosophique* (Art. Bien et Mal), he says:

"War carries off fewer mortals than small-pox. The scourge of war is transient, while that of small-pox always reigns throughout the world after so many others."

In his essay on the death of Louis XV, published in 1774, he suggests that the king's first supposed attack of small-pox at the age of 14, thirty years before his death from this disease, was really "petite vérole volante, which is not small-pox properly so-called." It is noteworthy that varicella, which the term "petite vérole volante" signifies, was first clearly distinguished from small-pox in 1767 by Heberden in the "Medical Transactions of the College of Physicians," which it is possible that Voltaire, owing to his interest in medical literature, may have read. Elsewhere (*Précis du Siècle de Louis XV*, Chap. XLI) he says that the king's attack was of the putrid or malignant type, and that several of his officers contracted the disease from him and died.

Voltaire himself, as I mentioned in the first part of my paper, was an occasional sufferer from malaria, and had obviously derived considerable benefit from cinchona,

as he remonstrates with Frederick the Great for refusing to take it during an attack, in a letter dated October 25, 1740, containing some verses ending with the following lines:—

“ Mais, dieux, aujourd'hui qu'il s'écarte
De la droite raison qu'il a !
Il esquivé le quinquina
Pour conserver sa fièvre quarte.”

He then instances the cure by this drug of the King of Sweden, who for a long time had obstinately refused to take it.

A mocking allusion is made elsewhere (*Dictionnaire Philosophique*, Art. Cartésianisme) to the Duchess of Marlborough, who refused to take cinchona during an attack of tertian fever because it was called “ Jesuits' powder ” in England.

Several references to plague are to be found in the *Essai sur les Mœurs* (Introduction, § II and XIX, Chap. XXIX, LXXV) as well as in the *Dictionnaire Philosophique* (Art. Air).

In his description of the epidemic in 842 Voltaire states that plague properly so-called is a disease peculiar to the inhabitants of Africa. He recognizes the importance of shipping in conveying the disease, and declares that plague would spread all over Europe but for the wise precautions taken at the ports (*Essai sur les Mœurs*, Chap. XXIX).

In his account of the Black Death he discredits the Chinese origin given it by Mézeray, who had attributed it to a shower of meteors, and points out that in the first place there has been no instance of meteors giving rise to plague, and secondly, that the Chinese annals make no mention of any contagious diseases until the year 1507 (*ibid.*, Chap. LXXV). As regards the origin of the disease Voltaire denies that the air and vapours arising from marshy ground are the vehicles of plague, though he maintains that numerous other contagious diseases are produced by exhalations from hospitals and cemeteries. He points out that if air or exhalations transmitted the disease, a south-east wind would soon have conveyed it to Paris from Marseilles, where there were nearly 70,000 deaths from it in 1720. The real vehicles of plague in his opinion are clothes and furniture (*Dictionnaire Philosophique*, Art. Air).

References to well-known epidemics of plague in Russia are to be met with in the *Histoire de la Russie sous Pierre le Grand* (Chap. XIX), where we read of the death of 9,000 men from the disease during the siege of Riga, and in Voltaire's correspondence with Catherine the Great, where an allusion is made to the Moscow outbreak of 1770-1772.¹ In a letter dated October 6-17, 1771, Catherine told Voltaire that “ burning fevers with and without spots were carrying off many persons,” and that she had authorized Count Orloff to take the most suitable measures to arrest the epidemic. In his reply (November 12, 1771) Voltaire suggested that the epidemic was the result of Catherine's victories over the Turks, who had brought the contagion in their clothing.

Before leaving the subject of epidemic disease reference may be made to Voltaire's allusion to the outbreak of scurvy which occurred in Anson's fleet during his voyage round the world, and caused the death of half the crews (*Précis de siècle de Louis XV*, Chap. XXVII).

Several passages in Voltaire's works refer to the overcrowding, cross infection, and generally insanitary conditions which were rife in the Paris hospitals, particularly in the Hôtel Dieu, during the eighteenth century (*Dictionnaire Philosophique*, Arts. Air, Charité; *Le philosophe ignorant*, § 26; *Correspondance*, Lettre à M. Paulet, April 22, 1768, *Fragments des Instructions pour le Prince Royal de* * * *), and

¹ For the contemporary account of this epidemic by Shafonski, F. G. Clemow's “ Notes on some past epidemics of plague in Russia ” (*Practitioner*, 1894, liii, p. 220) should be consulted.

formed the subject of a celebrated report by Tenon in 1788, ten years after Voltaire's death.

The following passage in particular deserves quotation :

"In these charitable institutions the drawbacks have often outweighed the advantages. A proof of the abuses attached to these houses is that the unhappy patients are often afraid of being taken there. The Hôtel Dieu, for example, was formerly very well situated in the centre of the town near the Archbishop's palace. Its situation at present is very unsuitable now that the town is so large, and four or five patients are heaped together in one bed. One poor wretch gives scurvy to his neighbour from whom he contracts syphilis, and an infected atmosphere spreads incurable diseases and death not only in the hospital which was intended to restore men to life but also over a large part of the surrounding country. M. de Chamouset, one of the best and most public-spirited citizens, has calculated that a quarter of the patients die at the Hôtel Dieu, an eighth at the Hôpital de la Charité, a ninth in the London Hospitals, and a thirtieth in those of Versailles. In the large and celebrated hospital at Lyons, which for long was one of the best administered in Europe, only a fifteenth of the patients died in ordinary years. It has often been proposed to split up the Hôtel Dieu into several smaller hospitals in a better situation and with better sanitation and ventilation, but the money for this undertaking has been wanting" (*Dictionnaire Philosophique*, Art. Charité).

Elsewhere (*Fragment des Instructions pour le Prince Royal* * * *) Voltaire says :—

"The hospitals of Lyons and Amsterdam are models; those of Paris are shamefully administered."

Voltaire's description of the Hôtel Dieu is amply confirmed not only by Tenon's report but by the following contemporary account in the *Encyclopédie* (Art. Hôtel-Dieu).

"It is the most extensive, the most populous, the richest and the most frightful of all our hospitals . . . Imagine a long row of adjacent wards in which persons suffering from all kinds of diseases are collected and where three, four, five or six are often heaped together in a single bed, the living side by side with the moribund and dead, the air infected by the exhalations of the multitude of unhealthy bodies which convey to one another the pestilential germs of their diseases . . . Some of these poor wretches leave the hospital with diseases which they did not have on admission and which they often communicate afterwards to those with whom they live. Others incompletely cured pass the rest of their days in a convalescence as cruel as the disease, and the rest die, except a small number who are kept alive by a vigorous temperament . . . Projects of reform have been made at different times but never carried into execution."

Some indication of the abuses prevalent in army hospitals is to be gained from the statement that "L'homme aux quarante écus" had inherited his wealth from a man who had been contractor to military hospitals and had grown fat by keeping the wounded on a low diet (*L'homme aux quarante écus*, Chap. XI). Again, in the story of *Jeannot et Colin* we read of a contractor for military hospitals—

"a man of great talent, who could boast of having killed more soldiers in a year than the cannon destroyed in ten."

On the other hand, we learn from the *Précis du Siècle de Louis XV* (Chap. XV) that the provision made for the wounded after the battle of Fontenoy was excellent.

"Never in the history of war had more care been taken to relieve the sufferings connected with this scourge. Hospitals were got ready in all the neighbouring towns, and especially at Lille, the churches were even employed for this worthy purpose. No help or comfort was wanting either for the French or their wounded prisoners. . . . The hospitals were so well managed that the officers preferred to be treated there than in private houses—a thing never seen before."

Of special interest is Voltaire's suggestion for founding a maternity hospital for unmarried women, which he makes in the essay entitled "Prix de la Justice et de

l'Humanité" (Art. VI), published in 1777, indicating, as it does, the humanitarian spirit which Voltaire's enemies are so apt to ignore.

Speaking of the edict of the French king, Henri II, which punished with death any woman who gave birth to a child without having it baptized, Voltaire remarks that it would be better to endow hospitals to help women who wished to be delivered in secret, as thereby the mother's honour and the child's life would be saved.

"Such hospitals," it is pointed out in a foot-note to the Kehl edition, "would have to be directed by medical men who would regard the unhappy women committed to their care merely as persons who had been guilty of a slight lapse for which they had already atoned. Their stay in hospital would have to be short, but if they had no other resources, they might be allowed to stay as workers or nurses. By keeping the children in these hospitals until a definite date and by teaching them trades and attaching gardens to the buildings and grounds that might be cultivated, their education might be made cheap and money saved to give them dowries."

Another example of Voltaire's humanitarian spirit is to be found in the following protest in the same essay (Art. XXV) against the insanitary state of contemporary prisons.

"The prisons at Madrid which have been built in the great square are decorated with a façade of fine architecture. A prison should not resemble a palace, nor should it be like a charnel-house. The complaint is made that most gaols in Europe are cesspools of infection which disseminate disease and death not only within their own grounds but in their neighbourhood as well. Daylight is absent and there is no ventilation. The prisoners have no communication with one another except by their pestiferous exhalations. They suffer a cruel punishment before sentence has been passed on them. Charity and a good police system should remedy this inhuman and dangerous negligence."

The crowded state of the Paris burial-grounds was best exemplified in the cemetery of Saint Innocent, which is described in the *Dictionnaire Philosophique* (Art. Enterrement) as

"a vast enclosure devoted to plague, where the poor who often die of contagious diseases are buried pell-mell, and dogs sometimes come to gnaw their bones; a thick, cadaverous, infected vapour is exhaled, which is pestilential in the summer heat after the rain; and almost side by side with this sewer are the Opera, Palais Royal and Louvre."

Voltaire then quotes with approval the example of Versailles, where as the result of a protest by a private individual, a small cemetery in an overcrowded parish was closed and the burial-ground transferred to another district. The individual in question was a M. Pacou, the author of a *Mémoire concernant le cimetière de la paroisse Saint-Louis de la Ville de Versailles*, to whom Voltaire wrote as follows:—

"Your essay in favour of the dead who are very cramped for space and of the living who suffer from their pestilential exhalations is certainly in the interest of the human race, and it is only the enemies of the living and dead who can oppose your request" (*Correspondance*, October 3, 1768).

In a letter to Paulet (*ibid.*, April 22, 1768), Voltaire speaks of the exhalations of the dead killing the living in the churches, and in his comments on the Black Hole of Calcutta (*Fragments historiques sur l'Inde*, Art. XII) he relates how at Saulieu, in Burgundy, the vicar with forty children attending their first communion, died from exposure to the exhalations from a grave recently opened in the church.

An allusion to the practice of burial in churches is made in the *Vision de Babouc* in which Babouc exclaims:—

"Do these people really bury their dead in the same place as that in which they adore their divinity? Are these temples paved with corpses? I am no longer surprised that pestilential diseases should often devastate Persepolis."

MEDICAL JURISPRUDENCE.

There is much to be found in Voltaire's works that will appeal to the medical jurist who is interested in the history of his subject, especially if it be borne in mind that the reform of criminal legislation in France was due to Voltaire (Masmonteil). The trials of Calas, Sirven and Montbailli, the revision of which constitutes the crowning glory of Voltaire, are particularly worthy of study in this respect. In both the Calas and the Sirven case, the medical experts appear to have been grossly ignorant and incompetent.

In the Calas case the report of the surgeon Lamarque has been described as "a model of solemn ignorance and pedantic imagination" (Allier). In the *Declaration de Pierre Calas*, Voltaire states that Lamarque, who had to examine the body of Marc Antoine Calas, had been prejudiced against Pierre, because on one occasion Lamarque had mistaken the right eye for the left and Pierre had drawn his attention to the fact. The same surgeon is accused by Donat Calas (*Mémoire de Donat Calas*) of having miscalculated by more than two hours the time of Marc Antoine's death, from examination of the stomach contents.

In the Sirven trial the expert is described by Voltaire as having as much knowledge of physics as the magistrate of jurisprudence (*Avis au public sur les Calas et les Sirven*), and this taunt appears to have been amply justified by the subsequent reports on the case by the celebrated surgeon and medical jurist Antoine Louis; as well as by the Montpellier Royal College of Surgeons and Faculty of Medicine (Galland).

Of still greater medico-legal interest is the Montbailli case, of which Voltaire gives the following description (*La Méprise d'Arras*).

"An enormously stout widow, aged 60, named Montbailli, of St. Omer, was in the habit of intoxicating herself with the poison so improperly called *eau de vie*. This fatal passion, which was well known throughout the town, had already involved her in several accidents, which had endangered her life. . . . One morning she was found lying on a little box near the bed with a fairly deep wound of the right eye caused by falling on the box. The face was livid and swollen, and a few drops of blood were escaping from the nose, in which a considerable clot had formed. It was obvious that she had died of apoplexy on getting out of bed. This is a very common end in Flanders among those who take much strong drink."

In spite of the medical evidence the Council of Arras condemned her son to be tortured and to be broken on the wheel after having had his wrist cut off, and his pregnant wife to be hanged and burnt after she had given birth to her child. The sentence was carried out in the case of the man, but the wife's relatives appealed to Voltaire, who laid the case before the Chancellor Maupeou. The case was retried and the Montbaillis were declared innocent.

In a letter to Elie de Beaumont (September 26, 1765), the barrister who defended the Calas and the Sirvens, Voltaire relates how, during the absence of the doctor, a man was accused of having assassinated his son, whose death was really due to a malignant fever, but brought an action against his judges on the return of the doctor.

The danger of attaching any credence to children's evidence is illustrated by the account of a trial of several persons at Lyons for rape and parricide, when a boy of 5½ years bore witness against his mother. It was finally shown that there was not a word of truth in the accusation, and that the boy had been suborned by two other children, sons of the accusers—an excellent example of the mythomania of Dupré (*Dictionnaire Philosophique*, Art. Criminalité; *Correspondance*, Lettre à M * * *, December, 1771).

Reference should also be made here to the story of Elizabeth Canning, which relates how a young woman who had gone to London to be delivered of an illegitimate child pretended that she had been imprisoned and starved by brigands (*Histoire d'Elizabeth Canning et des Calas*).

The difficulties and errors associated with the question of infanticide are admirably set forth in the following case reported in the *Dictionnaire Philosophique* (Art. Supplices).

"A dead new-born child is found. A girl is suspected of being the mother. She is put in prison and questioned. She replies that she cannot have given birth to the child as she is pregnant. She is examined by what are inappropriately called *sages femmes* and matrons. These imbeciles declare that she is not pregnant and that her swollen belly is due to retention of the after-birth. The poor wretch is threatened with torture, loses her head and confesses that she has killed her supposed child. She is condemned to death and gives birth to a child while her sentence is being passed. Her judges thus learn that sentences of death should not be passed lightly."

Of no little interest is Voltaire's attitude towards historical cases of poisoning. His article on poisoning in the *Dictionnaire Philosophique* commences with the words:—

"Let us frequently repeat useful truths. There have always been fewer cases of poisoning than has been asserted. It is almost the same as with parricide. Accusations have been common and the crime very rare."

A similar view is expressed in a letter to D'Argental (March 21, 1774), where he says that he has always distrusted the large number of poisoning cases with which chroniclers love to fill their works.

Such accusations of poisoning, he points out, were rife from the earliest times, as is exemplified in the story told by Livy that the doctor of Pyrrhus offered to poison his king for a reward (*Histoire de Charles XII. Préface*). Equally incredible was the accusation made several centuries later that £10,000 had been offered to a doctor to poison Charles II of England (*Essai sur les Mœurs*, Chap. CLXXXII).

Among the supposed cases of poisoning where Voltaire considered that death was more probably due to natural causes may be mentioned those of Charles the Bald (*Essai sur les Mœurs*, Chap. XXIV), Charles VI (*ibid.*, Chap. LXXIX, *Des mensonges imprimés; Des honnêtetés littéraires*), the Dauphin, son of François I (*Annales de l'Empire*, Charles Quint; *Dictionnaire Philosophique*, Art. Supplices; *Pyrrhonisme de l'Histoire*, Chap. XXXVII: *Correspondance*, Lettre à Gaillard, April 28, 1769), Pope Alexander VI (*Essai sur les Mœurs*, Chap. CIII; *Pyrrhonisme de l'Histoire*, Chap. XL), Madame, the daughter of Louis XIV (*Siècle de Louis XIV*, Chap. XXVI), the Dauphin, son of Louis XIV, his wife and sons, the minister Louvois (*ibid.*, Chap. XXVII), and Alexis, the son of Peter the Great (*Histoire de l'Empire de Russie sous Pierre Le Grand*, Pt. II, Chap. X).

In several instances of these supposed cases of poisoning Voltaire shows that the real cause of death was some acute infection, such as tertian malaria in the case of Pope Alexander VI, acute pleurisy in that of the Dauphin, son of François I, and an acute eruptive fever in those of the Dauphin, son of Louis XIV, his wife and son, and other persons of note (*Dissertation de la Mort de Henri IV*).

Poisoning on a wholesale scale, of which one of the earliest examples was the black death attributed to the Jews poisoning the wells (*Annales de l'Empire—Charles IV*), is also exemplified only to be discredited in the case of the Marquise de Brinvilliers, suspected of poisoning hospital patients (*Siècle de Louis XIV*, Chap. XXVI), and of the French soldiers accused by the English of using poisoned shot at Fontenoy (*Des mensonges imprimés*, § XII; *Les honnêtetés littéraires; Dictionnaire Philosophique*, Art. Histoire).

Voltaire shows that several substances such as bulls' blood (*Dictionnaire Philosophique*, Arts. *Empoisonnements*, *Tonnerre*), powdered diamond (*Siècle de Louis XIV*, Chap. XXVI; *Correspondance*, Lettre au Marquis de Courtivron, July 22, 1755), and human saliva (*Un Chrétien contre six Juifs*, § XXXVIII) did not possess the poisonous properties attributed to them.

Lastly, in connexion with medical jurisprudence, mention may be made of Voltaire's views on the question of unnatural offences. He discredits the statement that pæderasty was ordered by law in Persia (*Essai sur les Mœurs*, Introduction, § XI), and that it was sanctioned in Greece (*Dictionnaire Philosophique*, Amour Socratique), as well as the stories told by Tacitus and Suetonius of the unnatural depravity of Tiberius and Caligula (*Le Pyrrhonisme de l'Histoire*, Chap. XII).

In the essay entitled "Prix de la Justice et de l'Humanité" (Art. XIX), while stigmatizing the vice as low, disgusting and unworthy of man, he protests against burning as a punishment for sodomy, and exposing the offender to the insults of the lower orders, as was the custom in England. Similarly, in commenting on the practice of bestiality, condemned by the Jewish law (*La Bible enfin expliquée—Lévitique*), he maintains that the stake is too barbarous a penalty for the young peasants who alone are guilty of the crime, and hardly differ at all from the animals with which they associate.

VARIOUS DISEASES.

Apart from the diseases already mentioned, and passing allusions to such conditions as leprosy (*Dictionnaire Philosophique*, Art. Lèpre et Véroie; *Essai sur les Mœurs*, Chap. XIX; *Prix de la Justice et de l'Humanité*, Art. XII), stone in the bladder (*Le philosophe ignorant*, XXVI; *Les Oreilles du Comte de Chesterfield*, Chap. I; *Dictionnaire Philosophique*, Art. Puissance—Toute Puissance), lead colic and mercurial tremors (*Dictionnaire Philosophique*, Art. Art, Beaux-Arts), plica polonica (*ibid.*, Art. Schisme), hæmorrhoids (*Correspondance*, Lettre à Frédéric II, October 14, 1757, and rectal fistula (*Siècle de Louis XIV*, Chap. XXVII, *Dictionnaire Philosophique*, Art. Arrêts de Mort), the principal diseases which seem to have arrested Voltaire's attention, owing to their social importance, were mental disorders, including convulsive hysteria, alcoholism and the king's evil.

Voltaire's remarks on mental disease cannot fail to strike one as remarkably modern. In the *Dictionnaire Philosophique* (Art. Folie) he defines madness as the state of having incoherent thoughts with conduct of the same kind. Then, after stating that dreams are really a transient madness, he continues:

"Madness during the waking state is a disease which necessarily prevents a man from thinking and acting like his fellows. Not being able to manage his property, he is forbidden to do so: as he cannot have ideas suitable for society, he is excluded from it. If he is dangerous he is interned, if he is violent he is put under restraint. Sometimes he is cured by baths, bleeding or a régime . . . A madman is a sick person whose brain is suffering, just as a gouty patient is one who suffers in his hands and feet . . . One can have gout in the brain just as in the feet . . . I am sorry to think that Hippocrates prescribed asses' blood for madness, and am still more sorry that the 'Ladies' Manual' says that madness can be cured by contracting the itch. These are funny remedies which seem to have been invented by the patients themselves."

In illustrating the inaccuracy of Esquirol's statement that the insane in the eighteenth century were regarded as incurable, Sérieux¹ has recently quoted this passage among others to prove that the remedies employed included methods still in vogue at the present day.

In another passage, after relating the history of Saint Paulin, who caused a man possessed by the devil to fall from the roof of a church to the ground and thereby lose his life, Voltaire continues:—

"This is not the way we cure those possessed by the devil nowadays. We bleed them, bathe them, and give them gentle purges and emollients. That is how M. Pomme treats them, and he has effected more cures than the priests of Isis and Diana have performed miracles. As for demoniacs, who would say that they are possessed by the devil in order to

¹ *Archives internationales de Neurologie*, 1924, XVII^e sér., II, p. 105.

gain money, they are whipped instead of bathed" (*Dictionnaire Philosophique*, Art. Démoniaques).

Visions are distinguished by Voltaire according as they are the outcome of rascality or insanity. Those of the former kind he regards as the concern of the police, while the other kinds of vision are to be subdivided according as the subject is sick, when he should be treated by a doctor, or in good physical health, when he should be lodged in an asylum (*ibid.*, Art. Visions).

Numerous passages in Voltaire's works refer to that form of convulsive hysteria which was prevalent at the tombs of saints and ecclesiastics, especially the tomb of the Deacon Pâris in the cemetery of St. Médard (*Dictionnaire Philosophique*, Introduction, and Arts. Convulsions, Démoniaques, Ignace de Loyola, Lois (Esprit des), Possèdes, Superstition; *Histoire du Parlement de Paris*, Chap. XXXIX, LXIV, LXV; *Commentaire sur le Livre des délits et des peines*, § IX; *Traité de la Tolerance*, Chap. XX; *Essai sur les Mœurs*, Introduction, § XLVII; *Siècle de Louis XIV*, Chap. XXXI; *L'A, B, C*, 3e entretien; *Correspondance*, Lettre à Madame de Fontaine, January 16, 1757, Lettre à M. Colini, July 31, 1775; *Satires*, Le Russe à Paris).

The tombs in question were the resort of the lame, the blind, the deaf and sufferers from other infirmities, who flocked there in the hope that miraculous cures would be performed.

L'aveugle y court, et d'un pas chancelant
Aux Quinze-Vingts retourne en tâtonnant.
Le boiteux vient clopinant sur la tombe,
Crie Hosanna, saute, gigote et tombe,
Le sourd approche, écoute et n'entend rien.

(*La Pucelle*, III, 146.)

The fanatical scenes which took place in the cemetery of St. Médard

"caused so much scandal that the tomb of the deacon Pâris became the tomb of Jansenism in the mind of all honest folk." (*Siècle de Louis XIV*, Chap. XXXVII.)

A guard was placed in the cemetery, and thus gave rise to the celebrated couplet:—

De par le roi, défense à Dieu
De faire miracle en ce lieu.

(*Dictionnaire Philosophique*, Art. Convulsions.)

Notorious among the "convulsionaries," as these Jansenist fanatics were called, were Carré de Montgeron, whom Voltaire denounces as an ignorant and senseless debauchee (*Histoire du Parlement de Paris*, Chap. LXV), and Abraham Chaumeix, a former schoolmaster, who was instrumental in the temporary suppression of the *Encyclopédie* on the grounds of its being directed against monarchy, religion and the State (*Dictionnaire Philosophique*, Introduction aux questions sur l'*Encyclopédie*).

A still earlier example of convulsive hysteria is described in the *Essai sur les Mœurs* (Chap. XXXI), where an account is given of an epidemic of the kind which broke out at Dijon in 844 among those who prayed at the tomb of a Saint Bénigne. Voltaire quotes with approval the remarks made on that occasion by a bishop of Lyons, who said that

"Bénigne was a strange sort of saint to cripple those who resorted to him, and that miracles should be wrought to cure diseases and not to cause them."

The prevalence of alcoholism in country districts, particularly on saints' days, is described in the following passage in the *Dictionnaire Philosophique* (Art. Catéchisme du Curé) in a dialogue between Ariston and the curé. Ariston asks:—

"What will you do to prevent the peasants getting drunk on festival days? That is

their usual way of celebrating them. You see some of the men overcome by a liquid poison, their heads sunk on their knees, their hands hanging down, deaf and blind, reduced to a state much below that of animals, taken home tottering by their despairing wives, incapable of working next day, and often rendered ill and brutalized for the rest of their life. You see others whom wine has converted into madmen exchanging blows and sometimes ending by murder those disgraceful scenes which are the shame of the human race. How will you stop such an execrable practice in your parish?"

The curé replies:—

"I have made up my mind what to do. I shall allow and even compel them to cultivate their land on festival days after divine service which I shall hold very early. It is the idleness of the festival which takes them to the public house. Debauchery and murder do not take place on working days. Moderate work contributes to the health of the body and that of the soul. Moreover, work is necessary for the State."

A passage of a similar tenour illustrating the connexion between alcoholism and crime is to be found in another section of the *Dictionnaire Philosophique* (Art. Fêtes):

"It is doubtless the publicans who have invented such a prodigious number of festivals, the religion of the peasants and artisans consists in becoming drunk on the day of a saint whom they only know by this form of worship. It is during these days of idleness and debauchery that all the crimes are committed, it is the festivals which fill the prisons, and keep alive the archers, judges' clerks, criminal lieutenants and executioners. That is the only excuse for festivals among us. The fields of the catholics barely remain cultivated, while the heretics' fields which are tilled every day produce rich harvests."

The introduction of alcoholism into South America is described as follows in the *Histoire de Jenni* (Chap. IX):—

"Hardly any disease but that of decrepitude was known throughout South America before we introduced that *eau de mort* which we call *eau de vie*, and which gives a thousand different diseases to anyone who drinks too much of it."

The prevalence of alcoholism in Flanders has already been noted in the description of the Montbailli case.

Several allusions are made to the royal practice of touching for scrofula, which was introduced into England by Edward the Confessor and continued down to the time of Queen Anne. In the *Dictionnaire Philosophique* (Art. Ecouelles) we read of Louis XI at Plessis-lez-Tours sending for St. François de Paul to cure him of the results of his apoplexy.

"The saint came with the king's evil. The saint did not cure the king and the king did not cure the saint."

Although the ceremony was resumed by Queen Anne, the last English king who touched for scrofula was James II, who continued the practice in his exile at Saint-Germain (*Siècle de Louis XIV*, Chap. XV; *L'A, B, C*, 3e entretien). Commenting on the enlightenment of England compared with France in this respect Voltaire remarks:

"King William, Queen Anne, George I and George II never cured anyone of scrofula. Formerly if a king had refused to avail himself of this privilege, he would have caused the nation to revolt, but to-day (1760) the king who wanted to do this would make the whole nation laugh" (*Réflexions pour les sots*).

Elsewhere (*Essai sur les Mœurs*, Introduction, § XXXIII) after alluding to the refusal of William III to continue this practice, Voltaire says:—

"If ever England undergoes a great revolution which will plunge her into ignorance, she will have miracles of this kind every day."

In concluding this paper on Voltaire, in which, as in my study of Lucian,¹—his counterpart in classical antiquity—I have collected the passages of medical interest from his works, I would venture to maintain that Voltaire, the founder of modern history and the most representative figure of the eighteenth century, deserves the attention of the medical reader in that he was a powerful advocate of the profession and a relentless foe of quackery, while by reason of his keen intellect and wide humanitarianism he was well in advance of his time in matters relating to public health, medical jurisprudence and social medicine.

REFERENCES.

- ALLIER, R., "Voltaire et Calas," 1898. BAILEY, P., "Voltaire's relation to medicine," *Ann. Med. Hist.*, 1917, i, p. 54. DU BOIS-REYMOND, E., "Voltaire in seiner Beziehung zur Naturwissenschaft," 1868. BOISSIER, R., "La Mort de Voltaire (Etude clinique et rétrospective)," *Thèses de Paris*, 1916-17, No. 8. DELAUNAY, P., "Le monde médical parisien au XVIII^e siècle," 2^e édition, 1906. GALLAND, E., "L'Affaire Sirven," 1910. LANSON, G., "Les grands écrivains français: Voltaire," 1906; "Lettres Philosophiques de Voltaire: édition critique avec une introduction et une commentaire," 1909. MASMONTEIL, E., "La législation criminelle dans l'œuvre de Voltaire," *Thèse pour le doctorat*, Faculté de Droit, Paris, 1901. RATTEL, J. A., "Étude médico-littéraire sur Voltaire," *Thèses de Paris*, 1882-1883, No. 383. ROGER, "Voltaire malade, Étude historique et médicale," 1883. ROLLESTON, J. D., "Voltaire and English doctors," *Compt. rend. Ve Congrès internat. Hist. de Méd.*, 1925 (in press). TRONCHIN, H., "Théodore Tronchin," 1906.

¹ *Proceedings*, 1915, viii (Sect. Hist. Med.), 49-58; 72-84.

Section of History of Medicine.

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On a Romano-British Castration Clamp used in the Rites of Cybele.

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In the British Museum¹ is a remarkable and unique bronze instrument, found in the bed of the River Thames, near London Bridge, in 1840.² Its use has been obscure since its discovery. A solution of the problem is here attempted.

§ 1.—DESCRIPTION OF THE INSTRUMENT.

It consisted of two shanks, 11½ in. (28·75 cm.) long, joined at their distal ends by a hinge-joint, like a pair of nutcrackers. The shanks are rectangular in section and present four surfaces; the anterior and posterior surfaces are quite plain, about ½ in. (12·5 mm.) wide. The external and internal surfaces are about ¼ in. (6·25 mm.) wide, presenting on the external surfaces busts of deities and heads of animals, modelled in the round and projecting boldly; there are also some other structural details, described below. Each shank consists of the following parts:—

(a) *Half-hinge*.—This is now wanting. It was a separate piece of metal, united to the shank by a tenon-and-mortise joint and connected by means of a movable rivet-joint, with the corresponding half-hinge of the other shank.

(b) *Half-oval*.—This has its convexity directed outwards and extends from the half-hinge to the body of the shank. When the instrument is closed it forms, with that of the opposite shank, an elongated oval. On the external surface, just outside the half-hinge, is the bust of a deity facing anteriorly, but set obliquely so as not to interfere with the opening of the instrument. Both these busts are broken and bruised on their medial aspects. Immediately external to the bust and in contact with it, is the bust of a horse facing externally. At the junction with the body, on the anterior surface, are two parallel grooves set obliquely.

(c) *Body*.—This extends from the half-oval to the handle. There is a very slight concavity of the internal surfaces of the two bodies in both this specimen and that at Basel; this would prevent close apposition of the blades except at the upper and lower ends. The internal surface is deeply serrated throughout its whole length. This serrated area is about 6 in. (15 cm.) long, and the serrations, thirty-six in number, extend from the anterior to the posterior surface, but cannot interlock on closure of the instrument. If the substance to be compressed were thicker at its middle, this arrangement would enable even pressure to be maintained over the whole compressed area. The external surface presents, distally, four busts of deities in series and proximally, the head of a bull near the junction of the body and the handle; these all face externally. The deities represent the planetary deities presiding

¹ Room of Roman Britain. (Case D.) C. Roach Smith Collection.

² C. Roach Smith, "Bronze Forceps found in the bed of the Thames," *Archaeologia*, xxx, p. 548, pl. xxiv. *Collectanea Antiqua*, 1852, ii, p. 60. *Cat. Mus. London Antiq.*, 1854, pp. 12, 13, No. 29. *Illustrations of Roman London*, 1859, p. 72, pl. xxi. L. Lersch, "Planetarisches," *Jahrbücher des Vereins von Alterthumsfreunden im Rheinlande*, Bonn, 1846, viii, p. 146. K. Diltthey, *Ibid.*, liii, p. 7. Haug, "Die Wochengöttersteine," *Westdeutsche Zeitschrift für Geschichte und Kunst*, Trier, 1890, ix, p. 44, No. 31. T. Wright, *The Celt, the Roman and the Saxon*, 4th ed., 1885, p. 323. Franz Cumont, *Textes et Monuments Figurés, Les Mystères de Mithra*, 1896, ii, p. 432, No. 317. H. B. Walters, *Victoria County History*, London, 1909, i, p. 110, fig. 47; and reference to Soc. Antiq., MS. Min. xxxviii, p. 304. F. Haverfield, "Roman London," *Journ. Roman Studies*, 1911, i, p. 167, pl. xxi. Reginald A. Smith, *British Museum, Guide Antiq. Roman Britain*, 1922, pp. 86, 87, 21, pl. vi. B. C. A. Windle, *The Romans in Britain*, 1923, p. 190. Gordon Home, *Roman London*, 1926, p. 88, figured on p. 89.

over the eight days of the Roman week. The body of the right shank has been broken at its proximal end and neatly mended, by means of a mortised piece of bronze, in Roman times.

(d) *Handle*.—This is undecorated except at the proximal extremity, which terminates in a lion's head. The head forms an irregularly conical knob. The base of the cone projects on all surfaces except the inner, where it is smooth and flattened to permit closure of the instrument. The noses of the lions, however, do not come into contact and there is no grooving of the opposed flat surfaces, as might be expected had the instrument been intended for a forceps. The anterior and posterior surfaces are reduced in width to about $\frac{1}{4}$ in. (6.25 mm.), at the expense of the inner portion of the handle, and the angles between them and the external surface are chamfered. When the instrument is closed there is therefore a gap between the handles of the two shanks, designed to facilitate the grasp of the hand. About half-way between the lion's head and the body of the shank is an oblong perforation with rectangular section. This perforation was probably intended for a slightly curved connecting-bar passing between the handles. The margins of the perforations are worn from use. The perforation in an already narrowed handle was a constructional defect and a source of weakness, and the right shank is bent outwards as a result.

§ 2.—FUNCTION OF THE INSTRUMENT.

Mr. C. Roach Smith described it as of "forceps type," and stated that "the manner in which the forceps was used is not very clearly seen." He has been followed by others, who have described it as a "Zange" (Lersch, Diltthey, Haug) or "pince" (Cumont). It cannot, however, have been a forceps, as the front of the lions' heads do not come into contact, and the construction of the terminal knobs makes the instrument unsuitable for grasping any object. The projecting figures would also prevent it being grasped as a forceps or pair of tongs. Mr. Smith suggested alternatively that it might have been used for cracking or crushing objects, without indicating the nature of the objects to be compressed. The majority of the writers (Wright, Cumont, Walters, Haverfield, Reginald A. Smith, Windle) who have dealt with this instrument admit that its use is unexplained. It was formerly labelled in the British Museum as "A Pair of Brays for the Nose of a Victim."

Herr R. F. Burckhardt, Director of the Historisches Museum at Basel, writes that the somewhat similar instrument from Augst is "believed to be a nut-breaker or nut-cracker." Mr. Gordon Home calls the London example "nut-crackers." Professor Haverfield referred to it as "crackers." However, both instruments are quite unlike nut-crackers, with broad crushing surfaces, furnished with roughnesses to prevent the nut slipping, and with these surfaces placed quite near the hinge to obtain greater leverage. The Romans were quite familiar with the lever, and they would not ignore elementary mechanical principles in the construction of nut-crackers.

What, then, can have been the function of this instrument? It shows evidence of hard use, as the right shank was broken and mended in Roman times, and the margins of the holes for the connecting-bar are worn. Is it an instrument of torture? The old label in the British Museum suggests this. Professor Haverfield stated that it was "certainly not . . . a pair of brays for the nose of a victim." It seems hardly likely that so much elaboration and symbolism would be expended on a mere instrument of torture.

In its essential features it is not unlike certain clamps used in modern surgical practice (*e.g.*, in operations on the stomach and intestines) for arresting hæmorrhage, grasping soft tissues and maintaining them in apposition, where no great crushing force is required. This instrument had probably the same function in Roman times. The mechanism suggested for the connecting-bar is simple, and in use at the present time, but there are many other methods that might have been adopted to obtain the same result.

The cumbersome character and elaborate decoration are, however, arguments against its use as an ordinary surgical instrument. Surgical instruments in Roman

times were rarely decorated. The majority have only simple mouldings or are quite plain, permitting them to be cleansed easily.¹

Mr. C. R. Smith thought it "connected with the religious worship of the Romans," basing his views on the presence of the heads of deities. M. Cumont, guided in his opinion by the position of Cybele at the summit, said that it was "plus probable que . . . cette pince été en usage dans un temple de la Grande Mère." Mr. H. B. Walters emphasized its religious or sacrificial character, and stated that "the two busts on the top, probably Cybele and Attis, refer to the worship of the Phrygian Magna Mater."

An instrument so elaborate and costly was no makeshift. It was designed thoughtfully for the purpose in view. Evidence of prolonged use is seen in the repaired fracture, and signs of wear and tear. Everything suggests that the design was one that had proved satisfactory to the users.

It is therefore a clamp for controlling hæmorrhage and maintaining apposition of severed edges in soft tissues. The length of the serrated surfaces shows that the area of tissue to be controlled was an elongated one. The oval hole at the distal end must have had its use, as it adds nothing to the beauty of the instrument as regards its lines or to its efficiency as a clamp. As we shall find, it was a carefully thought out part of the design.

The only situation which meets all these requirements in that part of the human body with which Roman surgery dealt is the region of the male external genital organs. The suggestion here advanced is that this instrument is a clamp used in the operation of castration in the male, where the penis is excluded from operative procedure, i.e., the operation undergone by the "Spadones" in Roman times. In addition, the sacred emblems show that this castration was a part of some religious rite.

§ 3.—DESCRIPTION OF THE OPERATION.

The operation of castration can be performed by one of three principal methods.

(1) The testicles are alone removed by two incisions in the scrotum, one for each testicle. This method was rarely used by the ancients in operations on man.

(2) The whole of the external genital organs are removed. This method was adopted in the case of the "Castrati" in Roman times, and is that favoured in the Orient and Africa. It was attended by a far greater mortality, mainly from hæmorrhage, but also from septic poisoning and complications resulting from subsequent urethral stenosis.

(3) The penis is left intact, but the testicles and *fundus scroti* are removed, leaving the upper and back part of the scrotum. This method was adopted in the case of the "Spadones" in Roman times. It was the more usual, as being simpler and attended by much smaller mortality. It was doubtless the operation for which this instrument was used.

The operation was probably performed thus:—

The subject having been placed on his back with the thighs widely abducted, the clamp was opened, the penis passed through the oval ring, and the testes and *fundus scroti* drawn forwards between the serrated surfaces. The clamp was then firmly closed and the closure maintained by revolving the nut on the connecting bar until it touched the handle. By the presence of the oval ring the penis was fully protected from pressure and kept out of the way of the operator, and a larger amount of the scrotum with its contents was firmly clamped; complete control of all the blood-vessels with perfect adjustment of the severed edges of the skin of the scrotum was secured at the same time. The testicles and fundus of the scrotum in front of the clamp were then removed by a rapid stroke with a knife. The blood-vessels of the stumps of the right and left testicles were then perhaps closed by the application of the actual cautery. After this possibly a few sutures of flax were passed by means of a bronze needle.

The operation could be performed very rapidly. The danger was mainly from hæmorrhage; difficulty and delay were superadded by the tendency of the cut edges

¹ J. S. Milne, *Surgical Instruments in Greek and Roman Times*, 1907.

of the scrotum to retract and roll in, and of the stumps of the severed spermatic cords with their bleeding vessels to retract out of reach. It will be noticed how admirably these difficulties have been appreciated and met in the design of this instrument.

§ 4.—THE INSTRUMENT IN THE HISTORISCHES MUSEUM AT BASEL (No. 1907, 1505).

This was found at Augst, near Basel, in 1830. It is of bronze, 20 cm. ($7\frac{1}{2}$ in.) long. The shank consists of the same essential parts, i.e., half-hinge, a fenestrated portion, body and handle. There are, however, some important differences, e.g., the half-hinge is not a separate piece of metal, mortised to the next portion, but continuous with it; again, the fenestrated portion is not a half-oval, but a nearly circular foramen, partly formed by a prolongation downwards of the half-hinge and partly by a curving upwards of the first tooth of the serrated surface, so that when the instrument is closed a dumb-bell shaped aperture is formed. The body has sixteen large serrations: the highest is curved upwards, the lowest two converge, curving towards each other to form a similar, though smaller, incompletely circular foramen, situated at the junction of the body and the handle. This serrated area is about 8.5 cm. ($3\frac{1}{2}$ in.) long. The handle has no perforation and terminates in a knob. The knob is joined to the handle by a circular disc with an encircling groove: it is faceted, consisting of two four-sided pyramids joined at their bases, and terminates in another smaller disc surmounted by a similar but much smaller knob. The whole instrument is smaller. It is quite plain. The contour is angular, instead of rounded, opposite the fenestrated portion, from which point the body curves downward to join the handle.

The method of using the instrument is also different. The clamp has no aperture for the penis, which was probably held aside by an assistant while the clamp was applied to the scrotum. The use of the two pairs of foramina is uncertain. They were perhaps intended to assist in steadying the clamp and maintaining its closure during the operation by means of cords. The probable method of application of the cords is sufficiently indicated in the diagram.

It was therefore a simpler, cheaper and more primitive, though quite efficient instrument. It may have been a portable clamp, carried by one of the mendicant missionaries of Attis (Metragyrtæ or Cybebi) on his journey through the Alpine passes to the Gallic or Germanic tribes.¹

§ 5.—OCCASIONS FOR THE OPERATION.

The operation of castration was of Oriental origin. In ancient times, apart from disease, it appears to have been performed for a variety of reasons²; e.g.—

(1) *Martial reasons*.—As a symbol of subjection to a superior power it was common in Ancient Egypt and the Near East, but appears to have had no place among Roman customs.

(2) *Penal reasons*.—It was performed under the civil law in Rome mainly for sexual offences, such as adultery, rape and the performance of castration, when the latter had been prohibited, on the principle of the law of retaliation.

(3) *Provision of Choristers*.—The early performance of the operation arrested the onset of puberty and its accompanying changes in the larynx. The voice retained the character of that of childhood.

(4) *Provision of "Pathici" or "Paedicones"*.—These were employed as sexual inverters by the wealthy Romans and ministered to the vices of the wealthy Roman women. This class was composed mainly of "Spadones."

(5) *Provision of "Castrati"*.—These were used as attendants in the women's quarters in the houses of the wealthy.

¹ I am much indebted to the kindness of Herren Burckhardt and Major, of the Historisches Museum, at Basel, for supplying me with information and a specially-taken photograph of this hitherto unpublished specimen and also for their courtesy in allowing me to include a description and illustration in this paper.

² Richard Millant, *Les Eunouques*, Paris, 1908.

(6) *Provision of "Spadones."*—These were very largely employed in various capacities in the household and public offices mainly on account of their trustworthiness; their numbers and influence caused them to play an important part in the later history of Rome and Byzantium.¹

(7) *Religious reasons.*—It formed an essential rite in certain cults for priests and votaries.

For the first six reasons an elaborate, symbolic instrument would not be required. This clamp was therefore designed and used for the last category. It was probably the property of a priesthood of some cult in which emasculation was an essential rite, and was part of the temple furniture.

§ 6.—THE RELIGIOUS CULT CONCERNED IN THE OPERATION.

Castration was an Oriental operation; mutilation of priests and votaries in connexion with religious cults and fertility festivals had also its origin and home in Asia, among the Semitic races, whence it spread by a process of proselytism. It was a noticeable feature in most of the closely allied cults in Anatolia and Syria,² e.g., Phrygia (Attis-Cybele cult), Stratonicea in Caria (Zeus-Hecate cult), Ephesus (Artemis cult), Hierapolis-Bambyce (Atargatis cult), Hierapolis in Syria (Adonis-Astarte cult), whither pilgrims from Assyria, Babylonia, Phœnicia and Arabia came to the great festival. It was found in Cyprus (Adonis-Aphrodite cult), Egypt (Osiris cult), and Augustodunum in Gaul (Berecynthia cult). Instances of the association with fertility festivals and phallic cults of castrated persons, "eunuchs from birth" (cryptorchids, hermaphrodites), and the functionally impotent have been found in India, Pegu, Korea, the Congo, South Nigeria and South Africa. Castration was sometimes associated with religious asceticism in the Early Christian Church; in modern times the same practice is found in India amongst Hindus, Sudras and Brahmans and also in Russia amongst the Skoptzy.

It was a rite originally closely associated with the Semitic Mother-Goddess of the East, the Asiatic fertility-goddess, who was worshipped under so many different names with the special complex of the Divine Consort, Heliolatry and ceremonies arising from these ideas. In the case of the Cybele cult and some others the rite was probably engrafted on the simpler worship of the Great Earth-Mother of the Mediterranean basin.

Many suggestions have been made to explain this widely-spread rite. It may have been an imitation of the act performed on Attis, or a token of humility manifested by the created to the Creator, or a symbol of subjection, a characteristically Eastern conception, or again a votive offering of that which was held most dear—the sign of creative force. The priests of Cybele adopted the name of Attis; they personified the Divine Consort of the Goddess. The rite may have signified the union of the deities, a perverted form of the Sacred Marriage. The periodical fertilization was considered necessary in order that the Goddess of Fertility should efficiently carry out her functions of transmitting life to plants and animals. The severed members, cast at the foot of the image of the goddess, were gathered up and placed in the sacred subterranean chambers of the Sanctuary of Cybele, or buried, i.e., placed in the bosom of mother-earth. The female dress was adopted afterwards. As an early operation produced a feminine type, it may have been related to the matriarchal idea, an ecstatic craving for assimilation to the goddess. Or it may be in origin a form of sympathetic magic, the votary encouraging the vegetative processes by assuming the attributes of the great goddess of vegetation.

Whatever its origin or meaning, there is no doubt that castration was considered essential for admission into the priesthood. The connexion between the severed

¹ E. Gibbon, *Decline and Fall of the Roman Empire*, 1896, i, p. 382, ii, p. 245, iii, p. 360, ed. J. B. Bury.

² J. G. Frazer, *The Golden Bough*, ii, v, vi. L. R. Farnell, *The Cults of the Greek States*, 1909, ii.

external genital organs and the fertilization of the soil is illustrated by the appearance on Castor pottery¹ in Britain of cock-phalli, in which the phallus may be winged (Colchester), and is provided with the legs of a cock. The cock was an emblem of the Corn-Spirit and was closely associated with the worship of Attis and Cybele, deities especially connected with the growth of corn. It is not impossible that some of the representatives of the phallus, on sculptured stones, amulets, rings, &c., in the period of the Empire, may have reference to the cult of Cybele, so popular at that time, rather than to that of Priapus, a member of the moribund pantheon of Rome.

In the accounts of the cult of Cybele which survive, stress is laid on the self-mutilation of the priests and votaries. These descriptions relate to the great festivals, when the votaries, after a period of fasting, worked up into a frenzy by vertiginous ritual dances and wild music, passed into a state of hypnosis. The forcible suggestion of the priests and the prominent display of the necessary swords in the temple, as at Hierapolis, had then the desired effect. The worshipper perpetrated the act perhaps quite involuntarily. There was probably no pain and little hæmorrhage, judging from the results of operations under hypnosis and the parallel acts of mutilation described in other forms of ritual in modern Oriental communities.

In the intervals between the great festivals the mysteries were conducted in a quieter, less ecstatic fashion. It was probably then difficult for the novice to screw his courage to the sticking point when entering the priesthood. This was so far recognized that even at the great festivals the testicles of a ram or bull were sometimes offered to the goddess as a substitute. During these intervals, therefore, the operation was probably performed by another person, possibly the High Priest or Archigallus, armed with an appropriately decorated instrument, such as that with which we are dealing. It would be of advantage at such a time to be able to perform the operation very rapidly with the least possible suffering and loss of blood. In the legends two versions are given of the mutilation of Attis. In one the mutilation was self-inflicted, in the other it was performed by someone else. A parallel occurs in the rites of the Skoptzy, where, at the meetings of the sect, a neophyte sometimes mutilates himself, though more commonly he submits to the operation at the hands of an important official at some other time. In India also the operation is performed on the religious ascetic by another person.

It has been asserted that the priests of Cybele were Castrati, not Spadones, but the instrument does not support this view. It is, however, possible that there were grades of initiation, and that the complete operation was conducted in two stages. This procedure occurs amongst the modern Skoptzy.

That the third method of operation was the one adopted is also suggested by certain extant representations of Attis, and "dancing priests," in which the penis is present though the external genitals are puerile, and the general physique feminine.

The third method was the more suitable for self-mutilation, as it required less courage, was attended by less shock and hæmorrhage, and could be carried out with the swords kept in the temple for that purpose. It is difficult to believe that any votary could parade the city or take his prescribed part in the festival after total removal of the genitals.

There are many variations in the details of the operation as performed in modern times amongst different communities. Generally a tight ligature is passed around the root of the genitals. The use of a clamp seems unusual, but in India,² among Hindus, Sudras and Brahmins, who submit to the operation of total removal from religious motives, a split bamboo lath takes the place of the ligature. This lath is passed down by an assistant close to the pubes, embracing the whole of the

¹ Colchester and Saffron Walden Museums.

² John Shortt, "The Kojahs of Southern India," *Journ. Anthropological Institute*, ii, 1873.

external genitals at the root. The operator grasps the organs with his left hand, and removes them at one sweep by a sharp razor.

The cutting instrument varied greatly. The legends relate that in the case of Uranus a sickle, doubtless of flint, was used. Attis employed a sharp stone, probably a knife of flint or obsidian from Melos. The sword was employed in Hierapolis.

Our instrument is instinct with the operation. Cronus (Saturn) castrated his father Uranus, and suffered in the same way at the hands of his son Zeus (Jupiter). Aphrodite (Venus) was the product of the outrage by Cronus. Attis was the result of the castration of Agdistis, and the indirect fertilization of his mother Nana. In turn he was subjected to the same treatment at the hands of himself or others. Cybele, in her male personification as Agdistis, also went through the same ordeal. The rite was thus employed by a great number of different cults in some cases closely allied. The question arises, which of these Oriental religions introduced this clamp and employed it in Britain?

The religion of Mithras may at once be excluded, as castration formed no part of the Mithraic Mysteries. There is some evidence of the worship of Astarte, the Tyrian Hercules, and the Egyptian cults of Isis, Serapis and Osiris in Britain, but at this period there was so much syncretism of these Eastern religions, which had so much in common, that it is not easy to separate them from the dominant cult of Attis-Cybele. The presence of Attis-Cybele at the summit seems here absolutely decisive. The bulls and lions are Eastern motives, and though not restricted to any cult, are particularly associated with Cybele. The planetary deities seem also closely connected with her worship. The worship of Cybele syncretized with other Anatolian and Syrian cults. It had spread over the whole Empire, and was firmly established in Gallia and Germania. It must have extended to Belgic Britain, peopled by a race of Gallic and Germanic origin, with very close political and commercial connexions with the adjacent continent. It no doubt received in Britain, as in Gallia, a great stimulus in the second and third centuries of our era. We are therefore justified in assuming that this instrument was a castration clamp used by the Archigallus in the rites of Cybele, and that it formed part of the furniture of a temple of the Great-Mother in Londinium.

§ 7.—DATE OF THE INSTRUMENT.

The presence of the planetary deities gives a useful indication of the date of the clamp. The Astral cult, in which the stars, sun, moon and five planets ruled human life,¹ was of Eastern origin. It was associated originally with Babylonian astrology. Although there were traces in Rome from 159 B.C. or earlier, the quasi-scientific study of astrology dates from the birth of Augustus in 63 B.C.,² and seems to have reached its climax about the time of Antoninus Pius (A.D. 138-161). Though introduced into the Western world in association with certain Oriental religions, the planetary deities were identified with Western gods. In addition to other functions they were particularly associated with the days of the week from at least the first century of our era. Their employment in art appears in a calendar painted on a doorpost in the house of Trimalchio³ during the reign of Nero (A.D. 54-68), and in medallions in wall-paintings at Pompeii during the reign of Vespasian (A.D. 69-79). Though found in Syria, Egypt and Italy, their representations are especially noticeable in

¹ F. Cumont, *Textes et Monuments Figurés, Les Mystères de Mithra*, 1896. *Les religions orientales dans le paganisme romain*, 1906. *Astrology and religion among the Greeks and Romans*, 1912. J. de Witte, "Les divinités des sept jours de la semaine," *Gazette archéologique*, Paris, 1877, iii, pp. 50-57, 77-85. L. Lersch, "Der planetarische Götterkreis," *Bonner Jahrbücher*, 1844, iv, pp. 147-178; 1845, v, pp. 299-326. Haug, op. cit. A. Lang, "Star Myths," *Custom and Myth*, 1893. Salomon Reinach, "Dies," *Daremberg et Saglio. Dict. Antiq. grecques et romaines*, ii, p. 171.

² W. Warde Fowler, *The Religious Experiences of the Roman People*, 1911.

³ Petronius Arbiter, *Satyricon*, c. 30 (Cena Trimalchionis).

Eastern Gaul and Western Germany in the regions of the Rhone and Rhine. They are known also in Britain. Their appearance in the Rhine area can be dated from the reign of Nero,¹ but they occur more commonly in the reigns of Septimius Severus (A.D. 193-211) and the succeeding emperors.

In the western area the planetary deities appear usually in the same order as the tutelary divinities of the days of the week, ranged from left to right or right to left and commencing with Saturn. They are found on objects of a religious character, such as stone altars, funereal stelæ, the octagonal bases of the "Jupiter and Giant" columns, calendars and reliefs, and other objects of temple furniture, such as this clamp must be. They also occur on objects of a secular nature, and have then a talismanic function, e.g., tessellated pavements, vases of silver and bronze, pottery, and bronze circular amulets. In a symbolic form they appear on pre-Claudian British coins and Romano-British seals.

These considerations suggest that the instrument is post-Augustan, probably belonging to the second or third century.

§ 8.—PLACE OF MANUFACTURE OF THE INSTRUMENT.

This instrument and the specimen from Augst have the same general features. The Augst instrument is probably earlier and perhaps of local workmanship. The elaborate design, developed mechanical construction and fine workmanship of the London example render it unlikely that it was provincial work and suggest an origin in Rome or some Italian centre.

If made in Rome, it was probably intended for use in Britain or Western Europe, as it was ornamented with representations of the planetary deities.

The crudeness of the sculpture, the absence of definite symbols by which we might distinguish Keltic gods from those of the Romano-Greek pantheon, and the use of native pottery in the representations of the planetary deities prove that most of the objects of this type found in Gaul and Britain were of provincial manufacture. A few metal vases, figurines and other objects have been found that can only have been made in an Italian centre or by Italian craftsmen. Such is the case with our clamp, on which we note the definitely Roman character of the deities, each with the conventional symbol. M. Cumont² suggests that there was a regular trade in religious objects made in Rome.

The representation of eight planetary deities, in accordance with the eight days of the Roman week, is also suggestive; in the Keltic area the number is frequently only seven, even when symmetry demands an eighth member. The position of the presiding deities, too, is worthy of note; the goddess faces the right hand of the observer; in Eastern Gaul there are many native sculptures with representations of pairs of divinities of several different types, but in almost every instance it is the god that occupies this position.³

Moreover, the horns of the bulls also support the view of the Roman origin of this object. They are of the Roman or lyre-shaped type,⁴ as seen at Pompeii and in the majority of Romano-Greek representations, and are quite unlike those of the Keltic shorthorn (*Bos longifrons*) with the strong forward curve, the only domesticated variety in Britain before the Roman occupation.

¹ Mrs. A. Strong, *Journ. Roman Studies*, 1911, i, p. 23 (Jupiter and Giant column at Mainz).

² F. Cumont, *Les Mystères de Mithra*, 3me Ed 1913.

³ Émile Espérandieu, *Recueil général des Bas-reliefs de la Gaule romaine*, 1907 et seq. Salomon Reinach, *Cultes, Mythes et Religions*, 1922.

⁴ T. McKenny Hughes, "On the more important Breeds of Cattle," &c., *Archæologia*, lv, p. 137, fig. 10.

§ 9.—THE DECORATIVE FEATURES AND THEIR SIGNIFICANCE.

(a) *The Presiding Deities of the Cult at the Summit.*—Attis-Cybele. These two deities stamp the instrument as the property of the cult. They alone face the observer, as if supervising the rite. They are the only completely Asiatic deities represented. Their prominent position indicates that in religious matters the Orient has acquired complete ascendancy over the Occident, since the days when Rome, in her need, forsaking her own gods, sought the help of the Magna Mater of Phrygia in 204 B.C. The planetary deities are here identified with the gods of the Romano-Greek pantheon with Western garb and attributes. Accordingly, they occupy a subordinate position. Played out, as it were, they merely act as intermediary deities or serve to mark the flight of time.

The combination of the Divine Mother and her Divine Consort, on an equal footing, demonstrates that the primitive dominance of the Great Earth-Mother, the Virgin Goddess, complete in herself, has passed away. The cult has developed and Attis, the Anatolian god of vegetation, and consort of Cybele, is now the Sky-Father, the Sun-God, the Creator of all living things, the symbol of resurrection and a future life. He is united with the Earth-Mother, now also Queen of Heaven and Moon-Goddess. They possessed many attributes; but were essentially fertility-deities, different but complementary.

(b) *The Horses.*—These are evidently stallions, by their boldly arched faces and thick muscular necks. They may, perhaps, like the bulls, represent creative power. Their large size, prominent position, separation from the other animals and close association with the presiding deities suggest, however, a specially intimate connexion with Attis or Cybele, or both of them. They may, perhaps, represent the Sun-horse or the horses of the *biga* of Attis, the Sun-God. The symmetrical arrangement and association with both deities suggest some attribute common to both Attis and Cybele; perhaps they really represent the embodiment of the Corn-Spirit, as the production of corn was under the particular care of both deities. The importance of the horse in this respect was pointed out by Mannhardt,¹ whose opinion is supported, with reference to the "October-horse" and other instances, by Sir J. Frazer, Dr. L. R. Farnell, and the late Dr. W. Warde Fowler.² It seems not unlikely that the cult of the Horse³ in Western Europe, the horses of Epona in Belgic Gaul and Belgic Britain, some of the horses on Gallic and British coins, the equine deities of the Kelts, the horses cut in the turf of our chalk hills, and the horse-burials among the Parisii and Catuvellauni may be explained in the same way.

(c) *The Planetary Deities.*—The series reads from left to right, and begins with Saturn at the proximal end of the body of the left shank, passing up the body to the half-oval, and continuing downwards on the body of the right shank to its proximal end, as follows:—

Left Shank.

Dies Saturni (Saturday), Saturn (Cronus).
 Dies Solis (Sunday), Apollo (Sol, Helios).
 Dies Lunæ (Monday), Diana (Luna, Artemis).
 Dies Martis (Tuesday), Mars (Ares).

Right Shank.

Dies Mercurii (Wednesday), Mercury (Hermes).
 Dies Iovis (Thursday), Jupiter (Zeus).
 Dies Veneris (Friday), Venus (Aphrodite).
 Eighth Day of the Roman week.

¹ Mannhardt, *Mythologische Forschungen*.

² W. Warde Fowler, *The Roman Festivals of the period of the Republic*, 1899.

³ Salomon Reinach, "Vercingétorix à Alésia," *Cultes, Mythes et Religions*, iii, p. 139. "Les survivances du totemisme chez les anciens Celts," *Cultes, Mythes et Religions*, i, p. 30.

In representations of the planetary deities, whether having relation to the days of the week, as in calendars and certain monuments, or having purely tutelary functions, although arranged in the same order, as in amulets, &c., symmetry, the scheme of decoration, or plan of the object, may provide an eighth space. This eighth space is sometimes left blank, or is occupied by an inscription. Sometimes the space is filled by an additional deity, which is usually a Genius, Fortuna, Bonus Eventus, Felicitas, &c. In our clamp, Mr. C. R. Smith suggested Ceres, as she "equalizes the number on each side, and, at the same time, represents the old Roman week of eight days." The head is crowned with a calathus.

Saturn, bearded, wears a mantle draped like a hood. Apollo has a crown with rays. Diana bears a crescent moon at the vertex. Mars wears a plumed helmet. Mercury has a pair of wings at the temples. Jupiter, bearded, wears a crown of olive leaves. Venus has a stephane or diadema.

They are mostly deities connected with fertility in one form or other. It is surely no accident that, like the stallions and bulls, they are represented with their backs turned to Attis-Cybele and their faces averted from the scene of an act so fatal to reproduction.

(d) *The Bulls*.—From the dawn of pre-history, the bull has been regarded as the emblem of generative force. It was represented in this aspect by the Palæolithic cattle-hunter, as well as by the cattle-breeder of the Neolithic and Bronze Ages. As totem, symbol of a deity or object of sacrifice, it appears more frequently in religious representations than any other animal. It was, like the ram, sacred to Cybele; but was associated with Attis, in the same way as the lion was with Cybele.

(e) *The Lions*.—In the religion of Cybele the lion and bull association had a long ancestry, dating from the Minoan period, when Crete and Phrygia were closely connected, before the Phrygo-Thracian wave from Europe had passed over the earlier Anatolian population. The Great Earth-Mother was the Goddess of life and reproduction and also the Goddess of death. The bull symbolized the former attributes, the lion the latter. In addition, the lion assumed a particularly prominent position throughout the whole area influenced by the Earth-Mother and her successive phase as the Magna Mater of Phrygia. This lion was, however, a domesticated animal. Accordingly, lions appear as attendants, temple-warders, guardians of the tomb, anthropophagous animals, heraldic supporters, the draught-animals of her chariot, the seat on which she reclines, the arms or supports of her chair, and the animal which she caresses on her lap.

The general scheme of decoration has been planned very carefully; and yet is quite simple and full of meaning. It is no mere medley of heterogeneous ornament. If the instrument is held in a vertical position, the presiding deities of the cult, attended by their special Corn-Spirits, are at the summit. At the base are their symbolic animals. At the sides are the planetary deities, characteristic of the cult, acting as intermediaries between the celestial beings above and the terrestrial below. If held horizontally, the divinities encircle completely the area of the ritual act, except in the region of the handles, the terminals of which are provided with guardian lions. The design and the symbology of the instrument are as remarkable as the surgical technique.

§ 10.—THE FATE OF THE INSTRUMENT.

This instrument, then, was made in Italy and imported into Belgic Britain to form part of the furniture of a Temple of Attis-Cybele in Londinium, which was now a great commercial and administrative centre thronged with Oriental merchants and other devotees of the Great Mother. It was used, broken and repaired in the course of its history of perhaps nearly 200 years.

At length the time arrived when a new Oriental religion, which had been recognized previously by Constantine in the Edict of Milan in A.D. 313, became the official religion of Imperial Rome, in A.D. 323. The Oriental religions, which had supplanted the worship of the ancient Gods of Rome and Greece, had in turn to give way to Christianity, and the Sanctuary of the Magna Mater in Londinium doubtless shared the fate of the pagan temples elsewhere.

The temple was probably raided by the Early Christian iconoclasts and the clamp was broken intentionally. This seems obvious when one considers the force required to separate completely the mortised hinge from the shanks; this separation could not result possibly from any legitimate use or accidental fracture. It could be effected easily by opening the clamp and moving forcibly the shanks in a lateral direction far beyond the normal range of movement; e.g., by grasping the handles, and bending them laterally while the knee was pressed against the hinge. The right handle was bent probably at the same time, at the place where the perforation for the connecting-bar was situated, this being the point of greatest weakness. The same movement brought the medial portions of the busts of the Attis and Cybele forcibly into contact, with the result that they are bruised and broken on this aspect.

The broken clamp and the rest of the temple furniture were thrown, most probably, into the River Thames, near which there is some reason to believe that the temple was situated.

§ 11.—SUMMARY.

(1) The instrument was found in 1840 in the bed of the River Thames, near London Bridge.

(2) It is a ritual clamp for castration, by the method used for Spadones, i.e., eunuchs who retain the penis.

(3) It was used to clamp the scrotum before it was removed by the ritual knife.

(4) There is a clamp in the Historisches Museum at Basel, which was used for the same operation, but is of simpler structure.

(5) The clamp was the property of a priesthood in which emasculation was an essential rite.

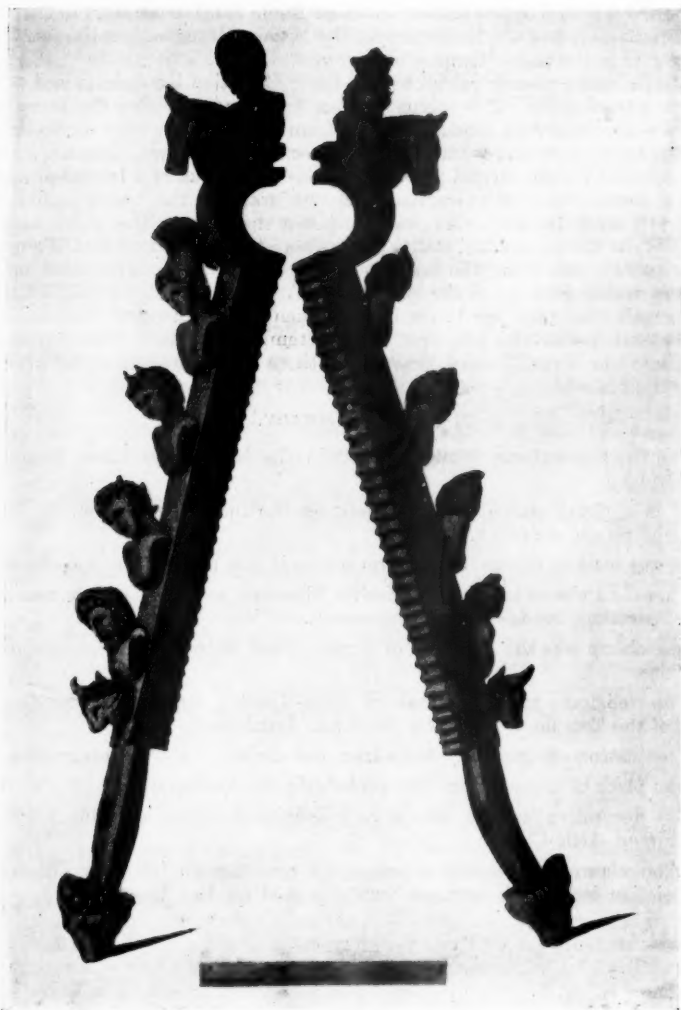
(6) The religious cult was that of Attis-Cybele; the clamp was part of the furniture of the Temple of the *Great Mother* at Londinium.

(7) The instrument probably dates from the second or third century after Christ.

(8) The place of manufacture was probably some Italian centre.

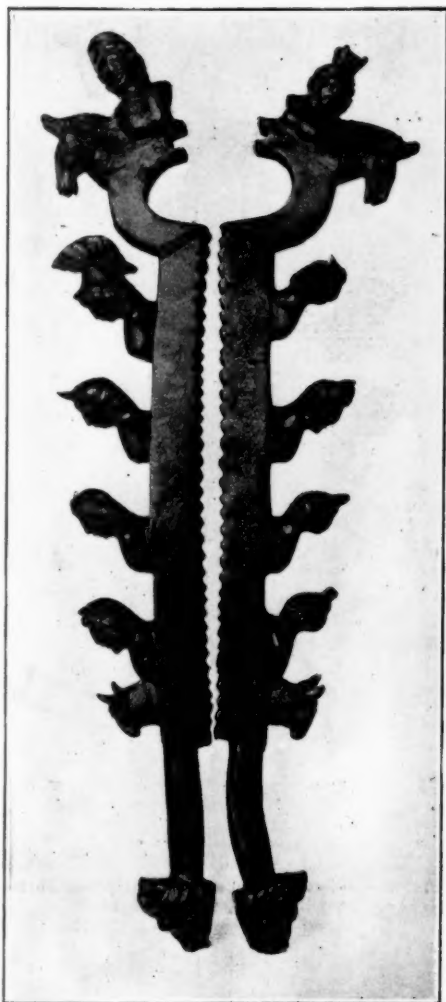
(9) The decorative features have a very definite symbolic meaning, suggestive of the worship of Attis-Cybele.

(10) The clamp was broken intentionally and thrown into the Thames by an Early Christian iconoclast, perhaps during a raid on the Temple.



By permission.

FIG. 1.—Bronze Clamp from River Thames at London. British Museum, Room of Roman Britain, Case D, from "A Guide to the Antiquities of Roman Britain," p. 86, plate VI. $\frac{1}{2}$ scale.



By permission.

FIG. 2.—Bronze Clamp from River Thames at London. Room of Roman Britain, Case D, British Museum. $\frac{1}{2}$ scale.

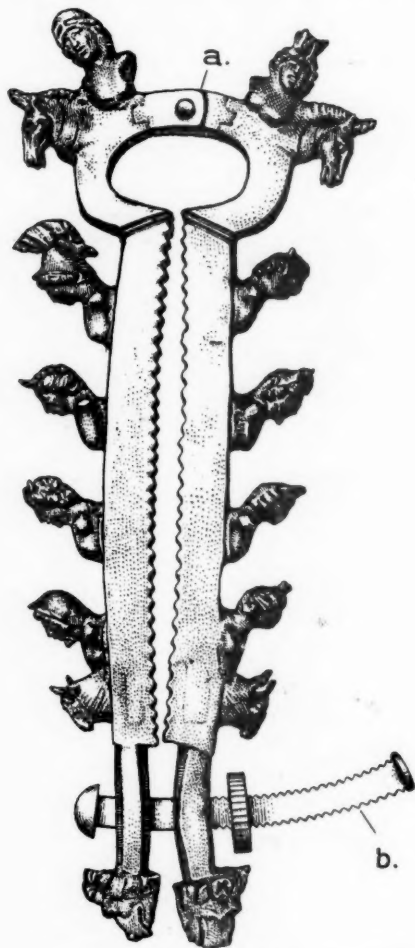


FIG. 3.—Conjectural restoration of Clamp from Thames.
(a) Hinge. (b) Connecting-bar.



FIG. 4.—Section of hinge in Fig. 3.



By permission.

FIG. 5.—Bronze Clamp from Augst, near Basel. Historisches Museum, Basel. $\frac{1}{2}$ scale. (No. 1907. 1505.)

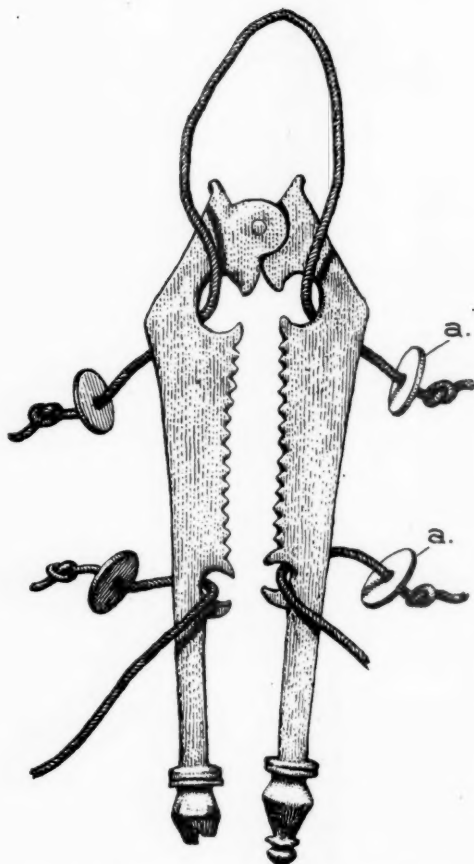


FIG. 6.—Clamp from Augst, fitted with knotted cords and metallic discs (a).

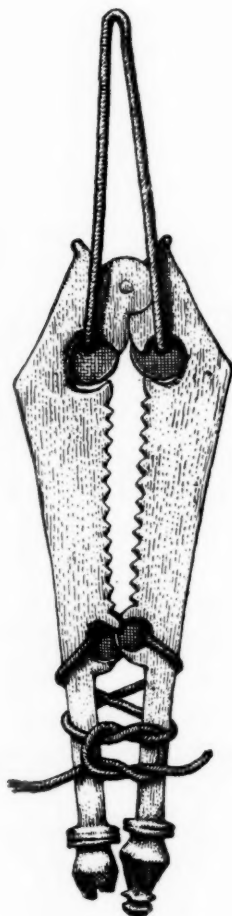


FIG. 7.—Clamp from Augst, closed, as for the operation.

[February 17, 1926.]

Glisson as an Orthopædic Surgeon.

By E. MUIRHEAD LITTLE, F.R.C.S.

FRANCIS GLISSON, born in Dorsetshire in 1597, entered Caius College, Cambridge; became M.D. in 1634 and F.R.C.P. in the next year. He was Regius Professor of Physic at Cambridge for more than forty years, and as such lectured on Human and Comparative Anatomy. He held the office of Censor in the Royal College of Physicians in 1656 and was elected President in 1667, 1668 and 1669. He stayed in London during the great plague of 1665 when many other physicians fled with their well-to-do patients. He died in 1677 at the age of 80 at his house in New Street, Shoe Lane,¹ and was buried in his parish churchyard of St. Bride, Fleet Street.

Besides the famous treatise on Rickets Glisson's published works are: *Anatomia Hepatis*, London, 1654, in which he described the "capsule" known by his name, the *Tractatus de Naturâ Substantiæ energetica, seu de vita naturæ ejusque tribus primis facultatibus*, London, 1672, a philosophical treatise, in which is an engraving taken from the portrait of him now in the Royal College of Physicians (fig. 1), and lastly the *Tractatus de Ventriculo et Intestinis*, London, 1676, which appeared shortly before the year of his death. All of his books were reprinted several times.

In the Sloane Collection in the British Museum there are twelve volumes of Glisson's manuscripts. Of these, two small volumes contain various letters to him, and some other papers. The other ten thick volumes contain notes and prefaces of his lectures, written some in Latin and some in English. A cursory survey did not reveal to me anything bearing on my subject, but a thorough study by anyone having youth, perseverance and familiarity with seventeenth century script might bear fruit.

Sir Norman Moore has adequately recorded Glisson's career and the history of the preparation and publication of his *Tractatus de Rachitide sive Morbo Puerile qui vulgo THE RICKETS dicitur*. In Moore's words it "will always remain one of the glories of English Medicine." It was the outcome of discussions among a number of physicians, who at length committed its preparation to a committee of three, namely, Francis Glisson, George Bate and Ahasuerus Regemorter. The two last named, however, soon left the work in Glisson's hands, reserving the right of final criticism and correction. So much is stated in the preface.

The first edition of the work on rickets was published in London in 1650 with the *imprimatur* of the Censors of the College of Physicians. The third edition, published at Leyden in 1671, has a frontispiece, interesting as containing representations of various deformities. In the foreground is a physician massaging or examining a crooked spine. In the middle distance a rachitic child is seated, and in the background is a child suffering from scoliosis or kyphosis playing cup-and-ball. On the wall hang preparations of bow-leg and scoliosis (fig. 2).

The English translation of the work, by one, Philip Armin, is dated 1651, and from this I shall largely quote. I have not been able to find out anything about Armin, whose translation is a very faithful one. A second edition of it is dated 1668, printed by John Streater and sold by George Sawbridge. It professed to be "Enlarged corrected and very much amended" by the notorious Nicholas Culpeper, but as the number and size of the pages are the same and the page on which each chapter begins is also unaltered, there cannot be any enlargement, and I cannot find either amendments or corrections.

¹There are three New Streets—Great, Little and Middle, as well as New Street Square and New Street Hill in that curious shut-in maze of streets and courts, bounded by Holborn, Fleet Street, Fetter Lane and Shoe Lane. I have not been able to discover in which of them Glisson lived.

²*St. Bart. Hosp. Rep.*, 1884, xx, p. 71.

Like many other discoveries, this of rickets was in fact a re-discovery. The disease was prevalent in Rome in the first century of our era and was described, but not given a name, by the physician Soranus of Ephesus.



FIG. 1

The word *Rickets* first appears in a Bill of Mortality of 1634, where it is given as the cause of death in fourteen burials. This number increased year by year until in 1659 it reached the surprising figure of 476 out of less than 15,000 burials, or three per cent. However, as the causes of death were reported by ignorant women

searchers, who probably did not see the patients alive, the figures can only be accepted with grave reservations.¹

Daniel Whistler in his *Disputatio Medica Inauguralis de Morbo puerili Anglorum quem patrio idiomate indigenae vocant THE RICKETS* published as an inaugural dissertation at Leyden in 1645, made no claim to the discovery of the disease. In 1645 the plan of Glisson's book was made public and Whistler apparently seized



FIG. 2

upon it as matter for his dissertation. The only thing original in it is the suggestion of the terrible word *Pædosplanchnosteccaces* as a name for the disease. Happily the author found no supporters.

¹ (Library of the Corporation of the City of London. Granger 5. 2. 3.) *Bills of Mortality*, 1602-66 Sir Clifford Allbutt (*Encycl. Britan.*, eleventh edition, Art. "Medicine") says that rickets was "first made known by Arnold de Boot, a Frisian who practised in Ireland in 1649." In view of the evidence of the Bills of Mortality, however, and of Whistler's inaugural dissertation in 1645, this statement cannot be accepted.

As Sir Norman Moore has said of Glisson: "To his description of the morbid anatomy as observable to the naked eye, subsequent writers, and even so laborious a pathologist as Sir William Jenner, have added little" (*Dictionary of National Biography*). Scarcely one of the usual symptoms of the disease escaped him. He even mentions its association with scurvy. As regards pathological causation he seems, however, to have been a thorough Galenist, and whole chapters of the treatise which deal with the triple constitution of the body, the spirits and the humors, indications and indicants and speculations as to whether it be a moist or a cold disease, are to the modern reader merely wearisome. He maintains that it is not a cold distemper, but a moist, and that "This Disease consisteth in the stupefaction of the Spirits" (chapter V).

The following account of the love affairs of the Vital and Natural Spirits may be taken as a specimen:—

"For when the vigorous vital spirits do meet together with the Natural spirits no less vigorous, they are united with a kind of curious strife and delightful contention. Whether that we may illustrate this matter by an example, the Natural Spirits as a Bride do here allure and in a manner repel the Vital Spirits who as it were act the part of a Bridegroom. But the Vital Spirits provoked with their heat, and driven on by the vigour of the Pulses do more confidently invade the Natural Spirits and penetrate into their confines and regions, whilst the

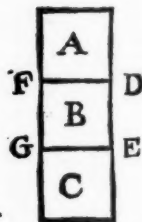


FIG. 3

natural spirits in the mean time (however as it were with modest resistances repulsing the assault) receive them at length not without a certain pleasure. For the very corporal pleasure is established upon and increased by a kind of amorous strife" (chap. XII, p. 101).

It must not be forgotten that the treatise was brought forth by a syndicate of physicians, and one may hope that the accurate clinical observations and sensible advice as to surgical treatment are Glisson's, while the fanciful physiology and pathology and the prescriptions of remedies containing worm-oil, earthworms, woodlice, stone-horsedung in a clyster and such like, are the work of Ahasuerus Regemorter and his fellows. Certainly there is a great contrast between the theoretical and the practical surgical sides of the book, which is probably typical of the state of the two branches of our art at the time. But where Glisson was not in bondage to systems and tradition, his surgical pathology was reasonable enough, even if his conclusions were not all justified by later experience.

He explains the curvature of the long bones by the hypothesis that there is overgrowth on the convex side and illustrates his theory with this diagram (fig. 3).

"We compare the bones therefore," he says, "in which this crookedness useth to happen, to a Pillar and not unaptly."

Then he says if you add material on one side you will make the pillar crooked as shown by the wedges in these diagrams (fig. 4). Further he says:—

"but if you build the pillar of more stones and betwixt every two as has been said, a wedge be interposed on one side, it will not resemble a Pillar, but the proportion of a Bow, as by the following may be perceived" (fig. 5).

"The Quacks of our Country," says he, "are wont to rub daily the hollow, not the convex sides of Bones, and that" (i.e. the former) "say they, doth very much conduce to the cure, but this" (i.e. the latter) "doth rather hinder it. But it is certain that rubbing doth powerfully summon the nutritive juice out of the Bloody mass into the part so rubbed, therefore if at any time you rub that hollow part which is insufficiently nourished, it is no wonder if it do good, being that thereby the aliment is more plentifully allured, and the heat of the part is also



FIG. 4

excited and augmented, neither on the other side is the gibbous part of the bone being hurt by rubbing, to be wondered at, because by that means the aliment is attracted to that part which was before superabundantly nourished."

He thus foreshadows the modern theory of massage.

Speaking of *genu valgum* and *genu varum*, which, however, he does not call by those names, he says:—

"And this bending seemeth to be not unfitly referred to the inequality of nutrition. For if it happen by unequal nutrition, that one side of the Shank-Bone be so lengthened more than the other: Suppose outwardly, that it doth somewhat lift up the outward part of the epiphysis of

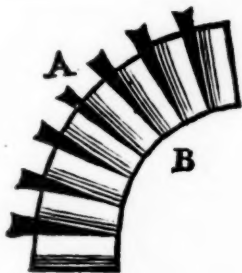


FIG. 5

the Shank-Bone [*Tibia* in original Latin] above the inward part, the joynt in the knee must needs stand outwardly bent; and on the contrary, if the inward part be lifted up, and the outward depressed, the same joynt must needs stand inwardly bent as may easily be perceived by the following figures" (fig. 6).

These figures need no explanation, but it may here be remarked that not until some forty years ago was the fact established that in rachitic knock-knee, deformity of the tibia was the most important condition, and not curvature of the femur as Macewen, differing from Glisson, had previously taught.

Glisson applies a similar pathological argument to deformities of the ankle and the bones of the spine, where it is less obviously correct. He says nothing of the effect of the weight of the body, of muscular contractions and tone, or of posture in causing deformity of too soft bones, probably because one of his very few omissions in symptomatology is this very softening, for he says :

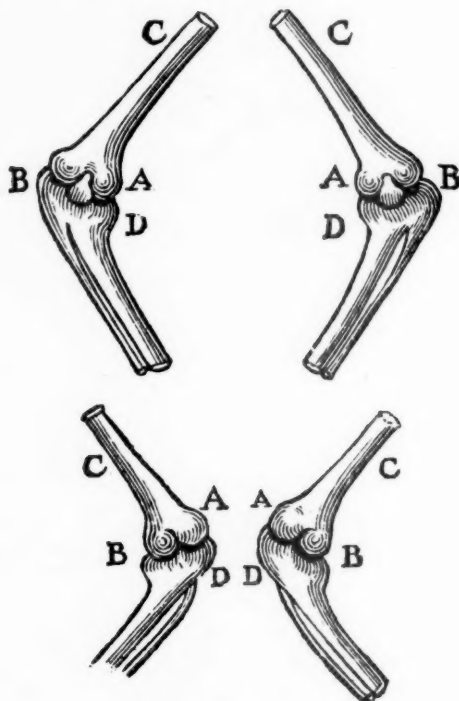


FIG. 6

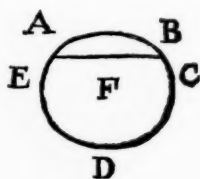


FIG. 7

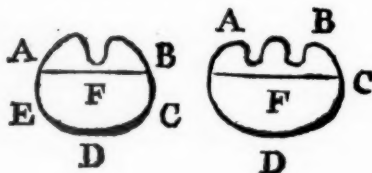


FIG. 8

"and first we flatly deny that the bones of children afflicted with this disease are more flexible, or less stiff and pliable than the bones of others" (chap. XIII). And again: "Some have imagined that the bones in this disease are transfigurable like wax; but we have never seen it."

The mechanism of the production of pigeon-breast Glisson explains with the help of figures. The sternum, he considers, is pushed forward by the enlarged liver and as you cannot push a part of a circular hoop outwards (figs. 7 and 8)

without drawing it in at other parts, the sides of the chest are narrowed. He meets the objection that the lower ribs are not drawn in laterally, but the opposite, by pointing out that they are not attached directly to the sternum, and do not form part of a complete circle. These ribs are kept distended by the large liver and bowels. Then he explains by diagrams (fig. 9), how the oblique muscles put into a state of tension by the bulky abdomen, draw the ribs downwards, and

"then they straighten the Breast on the sides."

Still arguing on his favoured hypothesis of deformity being caused by unequal growth, he says of the chest:—

"The cause of the vitiated Figure aforesaid, is an unequal nutrition of certain parts of the Ribs in respect of others."

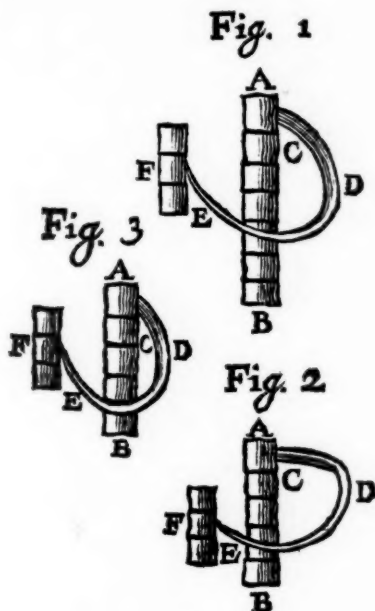


FIG. 9

He attempts to demonstrate this by means of a figure (fig. 10). Assuming that the ribs (the cartilages are not here mentioned) between *C* and *D* and the sternum, *A*, grow too much, compared with the parts *CB* and *DB*, he argues that the line of least resistance is in front, and that therefore they push the sternum forwards. As he was unaware of the softness of the bones and the effect of the contraction of the diaphragm and other muscles on them, his pathology is, however, here at fault.

Chapter XXIX is entitled "The Medical Matter answering to the indications proposed, and first the Chyrurgical." Here a curious surgical proceeding is discussed and recommended, namely scarification of the veins in the hollow of the ear. It is recommended to be performed two or three times a week, and is said to have a good effect on the fifth cranial nerve, and to "drive away the astonishment of the parts." *Astonishment* is used in its old sense of stupefaction, paralysis. Glisson says that the fifth nerve was affirmed by Fabricius Hildanus to be distributed

to the marrow of the back, and he evidently inclined to the belief that through it scarification of the ear might well be beneficial. The idea is an old one, and is to be found in both Greek and Arabian surgery. Issues also are approved.

Ligatures, if sufficiently loose and made of soft wool, are recommended. Glisson says

"this remedy is good to retard the over slippery return of the blood in those parts unto which the ligature is applied."

Slipperiness is often used in this treatise as a pathological term. In the original Latin it is *lubricatio*. Have we here a dim foreshadowing of the

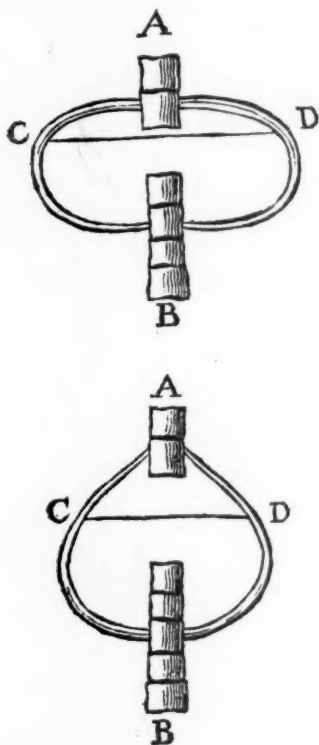


FIG. 10

congestion method of Bier? *Fasciation* or *swaything*, if not too tight, is also approved. He tells us also that

"others instead of swaything use buttoned Boots (*ocreas fibulatas*), lined with woollen cloth, . . . for strength and heat, but all to correct the crookedness of the bones. Some ad little shingles, or pieces of whalebone (*Aliqui fibulas addunt, aut particulas fissi ossis ceti*), but there are three things worthy of observation in the making of these:—

"(1) That they may somewhat crush the prominent and convex part of the Bone.

"(2) That they scarce touch the hollow, but rather that they defend it from compression.

"(3) That they be well fitted to the part, and do as little as possible hinder the motion of the joynts," &c.

"In like manner if there be any need that the Shingles upon the knee be extended to sustain and erect the bending thereof, then it is necessary that you fashion them with a double Joynt in the bending place after this manner (figs. 11 and 12).

"THE FORM OF THE ARTICULATION OF THE SPLENTS."

"A B Two Iron Rings."

"C D The Diameter of the Joynts of the Splents." (He means centres.)

"The Nails wherewith the Rings are fastened."

"F G The two Splents."

"Instead of the splents you may more commodiously use thin plates of Iron, and the whole instrument may be made of iron. The two Axel tress or diameters C D upon which the shingles or splents are bended F G are fastened with two rings or hoops" (i.e., discs.)

"But the hoops themselves, A B C, are made of plates of iron of an exquisite thinness, that they may not be burthensom, and withal they ought to be well smoothed and slight that they hinder not the motion of the splents. These rings must be of an equal latitude, suppose about two fingers across, and they must be so fitted, that on every side they may be parallels: only let there be so much difference between them that they may fitly receive the tops of the splents." (N.B.—If two finger breadths $1\frac{1}{4}$ in., then the diagram is half size.)

"Moreover, those hoops must not only be coupled with a double axel C and D, but also with five small Iron Nails. Lastly, the whole composition of the instrument must be so made,

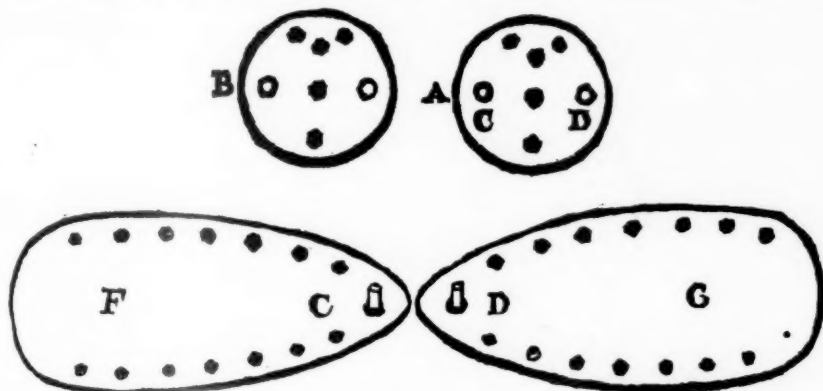


FIG. 11

that it may be fast and fitly tied to the side of the bended knee, sticking out, and withal that it may serve as well for the extension as the ordinary bending of it, but let it restrain the deflexion of it to either side, especially to the part sticking out. Which is the caus why the Axels are fastened with a double hoop, namely lest the Joynts should be loos, and yield to the deflexion of the knee. In like manner the torsion and misshapen writhing of the feet is also frequently corrected with swathing bands.¹ If the toes are outwardly distorted, they must every night be bound up, *little balls of cotton* being put between the heels and the ankles. But if the toes bend outwards, then you bind the ankles, and put a *little cotton*² between the great toes."

It seems doubtful whether or no the woollen cloth leggings and strips of whalebone could have much effect in correcting bow legs, but there is no doubt that the splints, if well made and fitted, would be efficacious in the gradual correction of *genu valgum* or *varum*.

Taking Glisson's measurement of two finger-breadths as being equal to one and three quarter inches, I have enlarged his drawing so that the discs are of that

¹ This is the first mention of foot deformity.

² In the Latin the word *pulvinar* is used, which would be better translated as "cushion" or "pad."

diameter; but, even so enlarged, the leg and thigh pieces are absurdly short for any but young infants. Evidently the diagram is not meant to be a working drawing. However, I have had an appliance constructed according to these directions. Presumably the dots round the sides of the splints represent holes for the attachment of padding. The arrangement of the joints on this splint is peculiar. It was probably adopted

Forma articulationis Ferularum.

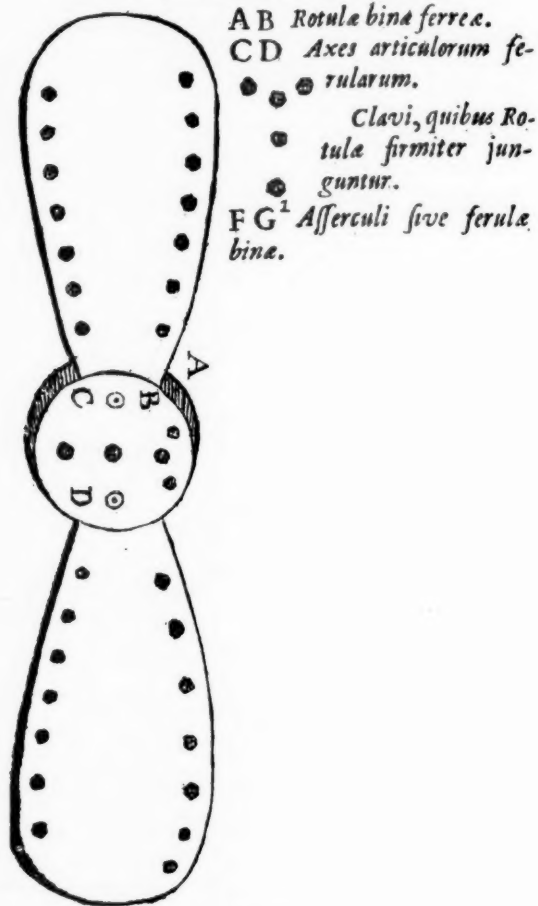


FIG. 12

with the mistaken idea of preventing lateral play, but it is interesting to note that the position of the two pivots would, when the splint was applied, roughly correspond to the two principal centres of movement during the last twenty-five or thirty degrees of extension of the knee, a joint which, as is well known, is a combination of a hinge with a sliding joint. This anatomical fact was not, however, known to Glisson.

¹ See fig. 11.

He says nothing as to the means of fixing the appliance to the limb, but no doubt bandages were used. It is noticeable that Glisson recommends that the splint be fixed on the inner side of a knock-knee, whereas modern surgeons would place it on the outer, thus distributing the pressure over two sites instead of only one. There must have been considerable risk of pressure sores with Glisson's method. He recommends also stays of woollen cloth stiffened with whalebone for the correction and support of curved or weak spines.

Chapter XXXII treats of *remedies electively evacuant*, and here we realize how difficult was the rôle of the conscientious physician, for he had not only

"to consider what remedies will electively expel the peccant humours in particular;" but also—"a due regard must be had to the spirits. . . . Moreover the predominant humours in the Body require proper and peculiar remedies; as Choler, Medicines purging Choler: Flegm, Medicines purging flegm: Melancholy, medicines purging melancholy; and waterish humors such as purge water."

Evidently an extensive pharmacopœia was needed to cope with all the possible or probable combinations of symptoms and indications. Luckily every plant, however humble, had its peculiar therapeutic value, and physicians were not restricted to the vegetable and mineral kingdoms, so that the liver of young ravens or of frogs was available, as well as

Wood-lice washed in white wine, baked in an oven, and beaten to powder, and such like things."

If anybody wants to experiment with the woodlouse treatment for rickets, let him remember that the dose is from half a scruple to a scruple, but perhaps an active principle might be extracted from this humble crustacean and called "oniscine"!

Chapter XXXV is headed "External Remedies," and begins by defining its subject as "every kind of medicament which cannot properly be referred to chyrurgery:" but it goes on to consider the manner or kind of exercises among which are included lying supine, prone or on one side. The use of pillows under the prominence to correct the "crookening" of the back while the child is in bed is recommended.

"The lying on one side towards the belly is laborious and troublesome and not to be continued long by strong and robustious bodies that are not used to it. But the molestation being overcome by custom, it is more easily tolerated: and because it easeth the pains in the head, helpeth the concoction of the Stomach, mitigateth the pains of the Chollick and loosneth a costive body, it may be sometimes useful when nature is thoroughly satisfied with sleep and in this affect it may supply the place of exercise." He cautions the reader against allowing patients to stand or walk too soon "for walking rather confirmeth than cureth the bended joynts."

"Moreover those children which have already contracted such a bending in their joynts, either by the natural weakness and loosness of the Ligaments, or by the bad usage or intelligence of their nurses, must not be trusted to exercise their legs till some splents or other instruments be provided, which may be able to erect the bended joynts and to keep them in an erected posture."

"Secondly, the artificial suspension of the body is performed by the help of an instrument cunningly made with swathing bands, first crossing the breast and coming under the arm-pits, then above the head and under the chin, and then receiving the hands by two handles, so that it is a pleasure to see the child hanging pendulous in the air, and moved to and fro by the spectators. This kind of exercise is thought to be many ways conducible in this affect, for it helpeth to restore the crooked bones, to erect the bended joynts, and to lengthen the short stature of the body. Moreover, it exciteth the vital heat and withal allureth a plentiful distribution of the Nourishment to the external and first affected parts: and in the meantime it is rather a pleasure than a trouble to the child."

I have myself slung up many children with Glisson's sling, but none of them seemed to like it!

"Some that the parts may the more be stretched, hang leaden shoes upon the feet, and fasten weights to the body, that the parts may be the more easily extended to an equal length. But this exercise is only proper for those that are strong."

This is "Glisson's sling," which in a simplified form is well known by that name to orthopædists, especially on the Continent. For instance, there are six references to it as "*die Glissonsche Schlinge*" in Albert Hoffa's *Lehrbuch der orthopädischen Chirurgie*. It is described, too, without acknowledgment by writers on Orthopædic Surgery of the eighteenth and the early part of the nineteenth century, such as John Shaw. It was subsequently adopted by Sayre, of New York, who probably knew nothing of Glisson's description. It is described in the form now used in a Latin inaugural dissertation by C. S. Braunert, *Historia machinarum ad gibbositatem sanandam*, Halle, 1798. Braunert speaks of

"*Machinae extensione agentes. Quem post apparatus Glissonius inventionem primo a se factam et escarpolette nominatam suo in libro (De rachitide, London, 1680) explanavit. Extremitates ligaminis longi lati atque validi, cujus medium sub mento et cervice agroti firmati transeunt cylindrum cubiculi tegumento insertum.*"¹

A quack some years ago widely advertised an apparatus which was constructed on the principle embodied in the above description and was guaranteed to increase the height of short people by several inches, or in the words of Glisson:—"ad curtam corporis staturam prolongandam conducit."



FIG. 13

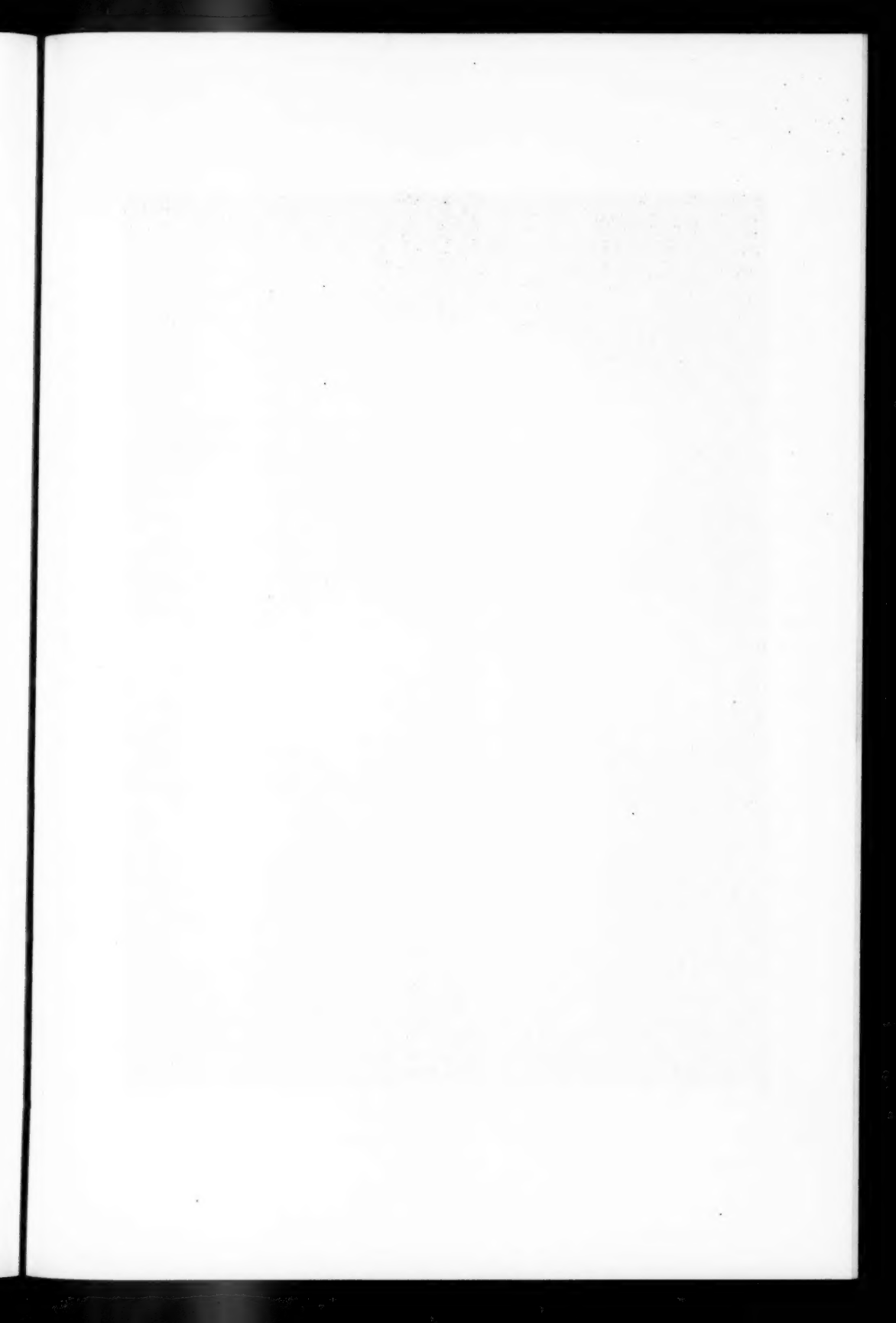
Besides these physio-therapeutic measures, frictions with the hand, a cloth or brush are recommended and abdominal massage of a quite vigorous sort is advocated, because

"Physicians hope, and not without reason, that by this action they may deliver the liver from any preternatural growing with the peritoneum, if any such should chance to be." . . . "Thus much of exercises, now follow the external Applications."

These are dealt with in Chapter XXXVII. The "things to be externally applied" include liquors, oyls, liniments, oyntments, playsters. Among these, muskadine, Prussian Beer, Oil of Neatsfeet and Foxes, Deers' suet, oyl of Worms and Goos-dung are noteworthy.

The shape of a plaster to be applied to the back seems to have been important. "Practitioners in Physick differ in the Figure and about the application of the Plaisters." Glisson (fig. 13) evidently thought the question important for he gives this figure as the best in some circumstances. "But when the lower parts of the backbone as also the knees and legs, namely those parts which borrow their nerves from the lower part of the spine, are weaker than the superior, we do not judge this latter to be a convenient form." After giving a final prescription for a liniment containing Oyl of Worms or human fat (*Adeps humanus*), he ends "And this much of external remedies."

¹ There is a copy of this Thesis in the library of the Royal College of Surgeons.





TWO SEVENTEENTH CENTURY "ANTIMONY CUPS."

One cup is shown in its original leather case. The polish of the lining of the other cup has been partially removed by the white wine which had stood in it for twenty-four hours.

Section of the History of Medicine.

President—Dr. J. D. ROLLESTON.

Antimonyall Cupps : *Pocula Emetica* or *Calices Vomitorii*.

By SIR STCLAIR THOMSON, M.D.

(President of the Society.)

"ANTIMONYALL CUPPS"—*Pocula Emetica* or *Calices Vomitorii*—are rarely met with nowadays. There is one in the possession of the Royal College of Physicians. It was presented to the College in 1824 by a Mr. Gurney, who had married a Miss Palmer, who was a descendant of the Dr. Baldwin Hamley to whom it originally belonged. The short story of it, compiled by Dr. Monk, states that it was bought in Gunpowder Alley, at the sign of the Magpie, in 1637, for 50 shillings, and that three cases of death were said to have been caused by the vomiting resulting from drinking wine which had stood in these cups. There is also such a cup in the Museum of Practical Geology in Jermyn Street. It bears on one side, on a shield surmounted by a coronet, the following inscription in German: "Du bist ein Wunder der Natur und aller Menschen sichere Cur."¹ The Pharmaceutical Society does not possess a specimen; nor is there one in the admirable Wellcome Museum in Wigmore Street, although it is the largest and most complete collection in the world of objects illustrating the history of medicine.

TWO EXAMPLES.

Hence I considered myself very fortunate when the opportunity came my way to exhibit two perfect specimens before the Section of History of Medicine. The record of these two particular "Antimonyall Cupps" is brief and inadequate. For the loan of them I am indebted to my old friend Mr. A. de Navarro, a well-known connoisseur in art. Amongst other things he collects pewter, on which he has written an interesting book, and he is at present President of the Pewter Society. It was in this connexion that he secured, through a well-known silversmith in Old Bond Street, as an addition to his collection of pewter, the two cups you see before you. Pewter is an alloy of tin and lead, but there are varieties. For instance, "plate pewter" consists of 89 per cent. tin and 7 per cent. antimony, fused with 2 per cent. bismuth and copper. It takes a fine polish. "Triple pewter" contains less tin and more antimony (15 per cent.). It is used in such minor articles as toys and syringes. "Lay pewter," used for inkstands, is composed of 80 per cent. tin and 20 per cent. lead. Hence some pewters contain no antimony, and none more than 15 per cent. Each of these cups is in an old leather case beautifully tooled, and when, inside each case, Mr. de Navarro noticed a label with the words "Antimonyall Cupp" he very kindly brought them to my notice, and has lent them for your inspection. The spelling and calligraphy are of the seventeenth century, as is also the leather case—possibly of Italian workmanship (see Plate).

You will notice that these cups must have had considerable use, if we may judge from the well-worn mark on the case, made by the thumb in opening and closing it. Each cup holds between 3 and 4 ounces of liquid.

EMESIS.

Emesis, or vomiting, is a therapeutic measure of wide and ancient use. Although nowadays chiefly employed by dogs and cats to "cleanse the stuff'd bosom of that

¹ A. C. Wootton, *Chronicle of Pharmacy*, London, 1910, vol. i, p. 385.

perilous stuff which weighs upon the heart," it was a relief to which most of us had recourse, involuntarily, in the days when we were "mewling and puking in the nurse's arms." With increasing years we employ it more rarely, and chiefly during a cross-Channel journey as a preparative for, or a corrective after, a week-end in Paris.

It was not so in classical times. Seneca writes that, in the reign of Nero, many "vomited to eat and ate to vomit." Cæsar, who was a temperate man, took an emetic after a heavy meal with Cicero, who mentions it without disapproval. Vitellius the glutton and Claudius habitually used emetics. But, in spite of these records, there are some students of the Roman age who say that daily vomits were not common in wider circles. The ancient Egyptians, according to Herodotus, were the healthiest of mankind, and three days in every month they used emetics and enemas. Hippocrates recommended regular vomitings and purgings. Asclepiades condemned them. Celsus disapproved of them as an aid to gluttony, but agreed that, as an occasional resource, they were conducive to health. Galen prescribed them before rather than after meals. Pliny and Plutarch only advised emetics in actual disease.

ANTIMONY.

To turn now to the metal of which these cups are made, we might recall that antimony was known to the ancients as "stibium," "barbason," or "albastrum."

As to its history, I wish time allowed me to make use of all the erudition and references so kindly placed at my disposal by our learned Fellow, Dr. Charles Singer. He tells me that the mediæval Latin word "Antimonium" was first used by Constantine, the African, who died in 1087. This Arab left North Africa for Salerno about 1070, became a monk, and translated medical works from Arabic into Latin. In one of these, the *Liber de Gradibus* (or Book of Degrees), the action of drugs is classified into four degrees, and antimony comes in the fourth or highest degree.

Many virtues were claimed for it and its derivatives. Ladies will be interested to hear that it was used in ancient times to beautify the eyebrows and give a dilated look to the eyes. Omphale, the Lydian queen who captivated Hercules, used "stimmi" for the purposes of the toilet; and it was possibly with a preparation of antimony that Jezebel "painted her face and tired her head" (2 Kings ix. 30). Anyhow, the "kohl" still used by females in Egypt and Persia is prepared from antimony.

As a remedy antimony owes its chief advance in medicine to the recommendation of Paracelsus (1480-1541), but it attracted little attention until the early part of the seventeenth century, when it was made popular by the enthusiastic writing of Basil Valentine, a monk of the Order of St. Benedict, who published at Leipzig in 1604, and in German, a work entitled "Triumph Wagen Antimonii," translated into English in 1678 under the title of "The Triumphant Chariot of Antimony." The author included antimony amongst the seven wonders of the world, and ascribed to it extraordinary virtues.

A vast literature has arisen round this Basil Valentine, but I have the authority of Dr. Singer to state that Basil Valentine the monk never existed, and that the book of which he is the reputed author was written by a certain Johann Thölde, of Hesse, a chemist and salt manufacturer. This astute chemist added to the interest and mystery by saying he had, with great labour, translated the monk's work from Latin into German. Anyhow, the work was translated into many languages, and the boom in antimony was launched and in full swing through the seventeenth century. Charles de Lorme appears to have made a huge practice and much renown by prescribing it to Henry IV, Louis XIII, Cardinal Mazarin, and Madame de Sévigné. He claimed for it that "qui plus en boira, plus il vivra"! and it is true

that amongst his patients were Guez de Balzac who died at 70, Boileau who died at 75, and Daniel Huet who reached the age of 91, while he himself nearly became a centenarian.

As a striking example of this fulsome laudation by an unqualified practitioner I can recommend the perusal of a pamphlet published in London in 1642 by "John Evans, Minister and Preacher of God's Word, dwelling near the Golden Lyon in Fetter Lane." Its title is:—

"The Universal Medicine, or the Virtues of my Magneticall or Antimoniall Cup. Confirmed to be an health-procuring, health-preserving, and an health-restoring Effectuall Medicine.

By extant Monuments of Antiquity.

By testimonies of Honorable Personages.

By 100 admirable and rare experiments.

By 200 Persons of quality that have experienced the same."

I am sorry the Royal Society of Medicine does not possess a copy of this egregious pamphlet, but it can be seen in the Library of the Royal College of Physicians. Mr. Barlow, the Bedell, has kindly called my attention to it, pointing out how the testimonials from the "persons of quality" closely resemble those issued by quack-medicine vendors in our own day. The reverend author, who repeatedly protests that he is ready to "answer before God and Man," in regard to the "Mystical and Celestiall" qualities of his vinum antimonialie was not free from personal interest in making "a Compendious declaration of the most admirable Virtues of the Magneticall or Antimoniall Cup," for he adds that it was "compounded and made of the Philosophical composition, which is of my own proper and peculiar Invention and Preparation."

The Rev. John Evans cited "ancient Philosophers and learned Physicians" who had "written of the Medicinall vertues of this Magneticall or Antimoniall Cup," beginning with Theophrastus Paracelsus and including Basilius Valentinus. This did him no harm, as Paracelsus was dead and Basilius Valentinus had never existed. But, unfortunately, he added that "Sir Theodore Mayerne, Kt., and Dr. of Physick, and Physician in Ordinary to the King's most excellent Majesty, hath approved and experienced the same oftentimes with happy and good success."

Now Turquet de Mayerne was a French (or possibly a Swiss) physician who had been "struck of the register" by the Faculty of Medicine of Paris in 1603, simply because he was a supporter of antimony, and even although he was the favourite physician of Henry IV. He settled in London, was appointed Physician to James I, became a Fellow of the Royal College of Physicians, and it has been suggested that he is portrayed by Shakespeare as "Dr. Caius" in the *Merry Wives of Windsor*. If so, it must have been a caricature, for his behaviour in regard to this unauthorized use of his name, in an advertising pamphlet by the Reverend John Evans, was very different from what one would expect from such a figure of fun as the physician in the *Merry Wives of Windsor*. De Mayerne promptly took action. There is a book written by Dr. Charles Goodall in 1684 on "The Royal College of Physicians of London," with "an Historical Account of the College's proceedings against Empiricks and unlicensed Practisers in every Princes Reign from their first Incorporation to the Murther of the Royal Martyr, King Charles the First." Well, on page 442 of this book, and under the date of "24 Martii 1634," we read the following Minute:—

"Mr. President desired that diligent search be made after the sellers of purging Diet-Ales and such Comfit-makers as sold purging confections. Dr. Mayerne wrote a Letter to Mr. President complaining of Mr. Evans a Minister who had abused his name about his Antimoniall Cup; upon which 4 Fellows of The College were sent to the Archbishop of Canterbury to acquaint his Grace therewith, and with the import of Sir Theodore Mayerne's

Letter. After this Evans was brought before the High Commission, where the Archbishop asked him for his Orders, which he had not then present. He then caused him to be sworn to answer such Articles as should be objected against him. His Grace was highly displeased at the printing of his Book, of which all that could be found were taken away. The College Beadle was to help to find out more, that they might be destroyed. Sir *Nathanael Kitch* died of a Vomit made by this Antimonial Cup. The Lady *Amye Blunt* died by the Same Medicine in *Charter-house* yard. Another case of the same kind was reported by Dr. *Harvey*."

This precious pamphlet of Mr. John Evans must have been largely responsible for producing in 1651 (just nine years later) a counterblast from "James Primrose, Doctor of Physick." This "learned physician" had the courage to attempt the Sisyphean task of exposing "Popular Errors, or the Errors of the People in Physick: Profitable and necessary to be read by all. To which is added by the same Author his verdict concerning the Antimonyall Cuppe."

This delightful little book can be read in our library. It gives some shrewd knocks to the Rev. John Evans in the last chapter, where Dr. Primrose writes:—

"Not that I doe altogether dislike the use of Antimonie, for I have often used it with good successe, but better prepared. But especially the founder of the Cup is to be blamed, for selling such a cheap medecine at so deare a rate, the right use whereof hee doth neither teach the people, nor I think he himself knowes."

That Evans is here referred to is clear from the next paragraph, where Dr. Primrose ironically says:

"As for the Founder of the Cup, he professes himself a Minister, and Preacher of God's Word, that is, a man that will scorn to deceive anybody and will not meddle beyond his knowledge."

The courage of Dr. Primrose is to be admired. It must have helped to the undoing of that unctuous humbug the Rev. John Evans. We may also congratulate Sir Théodore Turquet de Mayerne and the Royal College of Physicians on their successful action. The leaders and guardian bodies of the profession in those days appear to have been more successful than we are in their suppression of self-seeking frauds.

The controversy about antimony raged in Paris for over a century, dividing the profession into two camps—the antimonialists and the anti-antimonialists—causing, according to the habits of the times, the bitterest personal animosities and recriminations. It is referred to by Molière in *Le médecin malgré lui*. The vogue in the drug—fostered by writings like Basil Valentine's "Triumphal Chariot of Antimony," and Evans's "The Universal Medicine"—led to such popular recklessness in its use that the Faculté was possibly justified in declaring it a poison and reprehending its administration. In 1609 another eminent physician, Paulmier, was expelled from the Faculté for having administered antimony. This prohibition, confirmed by a solemn Act of Parliament in 1566, brought forth calmer judgments, like those of Dr. Primrose, and, possibly, confidence in the merits of the remedy was partially restored by the alleged cure of Louis XIV by tartar emetic for a dangerous illness in 1657. Anyhow, in 1666—just a century after its prohibition—another equally solemn Act rehabilitated the reputation of the metal.

POSSIBLE ORIGIN OF THESE CUPS.

I wonder if the prohibition of antimony during a whole century had anything to do with the origin of *Pocula Emetica*, *Calices vomitorii*, or Antimonial Cupps? The use and sale of the drug were interdicted by law, and knowing human nature as we do, and realizing how the banning of any man or his methods at once makes a hero of him and a panacea of his nostrum, it is possible that these cups came into being in that way. Wine being allowed to stand for some time in one of them became impregnated with tartrate of antimony, from the action of the tartar contained in the wine upon the metal of the film of oxide formed upon its surface. Now, as the

prescribing and selling of antimony was forbidden, these cups effectually set legislation at defiance, added the spice of a forbidden drink to the virtues of the draught, saved the apothecary's bill, and must have appealed to imaginative patients as an agreeable—being alcoholic—mode of administration! The cup, too, could be handed down from generation to generation, gathering increased powers of suggestion with the years.

It is said that these cups were common in monasteries, and those monks who took too much wine were punished next morning by having to drink some more which had been standing in a poculum emeticum.

AN ANCIENT RECIPE FOR ANTIMONIAL WINE.

I might explain that what in those ancient days was called "*Regulus of antimony*" is what we call metallic antimony, to distinguish it from crude antimony. Now, in Pomet's *Compleat History of Drugs*, of which the English translator says in the third edition of 1737 that it is "a work of great Use and Curiosity," we note, amongst much quaint lore, the following reference to *Pocula Emetica* on page 360:—

"Of this *Regulus* is prepar'd the purging or rather the emetick wine: And here you ought to be caution'd to throw away the three or four first wines you make with the Cups, lest they should produce some ill Accident. Whereas most People who have Occasion for the Goblets or Cups of the *Regulus* find difficulty to come by them, let them apply to a Founder, and they will have what Sorts and Sizes they will, at a cheap Rate, without troubling themselves with Moulds, as several have done to their Labour and Cost, who have at last been oblig'd to give over the Attempt, not being able to make one Cup without a Hole or some other Defect. You may also get these same Founders to make you the perpetual Pills, or you may easily make them yourself with a Musket Ball Mould."

Perpetual Pills.—"The Pills serve for those that have the Twisting of the Guts, or *Miserere mei*, so call'd. When they are returned from out of the Body, 'tis but washing and cleansing of them again, and they'll serve as oft as you please; which gives them the Name of Perpetual. They may also be infus'd, as well as the *Regulus* in Wine, cold, for the space of twelve Hours; which is said to be a good Medicine for strong Constitutions."

ORIGIN OF WORD "ANTIMONY."

The original work ascribed to the mythical Basil Valentine was published in Latin under the title of "*Currus Antimonii Triumphalis*," and his name, of course, was Latinized into *Basilius Valentinus*. It is to the author's investigations with this mineral and its products, carried out in a thoroughly scientific and Teutonic fashion, that we owe the ridiculous story as to the origin of the name of Antimoine or Antimony (against monks). The origin of this title is described in Pomet's work in the following words:—

"It acquir'd the Name of Antimony, according to the Opinion of some, from a *German* monk, the aforesaid *Valentine*, who in Search after the Philosopher's stone, was wont to make much Use of it for the more ready fluxing his Metals, and throwing a Parcel of it to some Swine, he observ'd that they had eaten it, and were thereby purged very violently, but afterwards grew the fatter upon it; which made him harbour an Opinion, that the same sort of Cathartick, exhibited to those of his own Fraternity, might do them much Service: but his Experiment succeeded so ill, that everyone who took of it died. This therefore was the Reason of this Mineral being call'd *Antimony*, as being destructive of the Monks."

CHEMICAL COMPOSITION OF THE CUP.

For the definite proof that these cups are actually made of antimony I am indebted to the kindness of Sir Herbert Jackson, K.B.E., formerly Professor of Chemistry in King's College and now Director of the British Scientific Instruments Research Association. A very small quantity of material, scraped from the bottom of one cup, was sufficient for him to apply tests which prove that the cup is made almost entirely of commercial antimony. There can only be, he reports, very small

quantities of tin and lead. The cup is a good specimen of metallic antimony. The metal is fairly hard and brittle, just as antimony is.

THEIR POWER OF PRODUCING ANTIMONIAL WINE.

Finally, to settle the question whether the antimony of which these two cups are made could be dissolved out into wine allowed to stand in them, I again had recourse to the learning and kindness of Sir Herbert Jackson; his report is as follows:—

"The white wine which has stood in the antimonial cup for seventeen hours contains a notable amount of antimony. No quantitative determination of the amount has been made, but, looking at the antimony separated from the wine, a rough estimate would be that there is about half a grain of antimony, expressed as antimony oxide, to the ounce of wine. I lay no stress on the quantity, but what I know you were anxious to learn is whether a wine of such character standing in the antimonial cup would dissolve an appreciable amount of antimony; it clearly does."

As I have noted, each cup holds 3 to 4 ounces, so that the wine would contain a dose of $1\frac{1}{2}$ to 2 grains of antimony.

CONCLUSION.

In one of these cups I have had some white wine standing for exactly twenty-four hours. If anyone would like to quaff it he is very welcome to do so at his own peril. You will notice how it has removed the polish from the inside of the cup.

Having now proved the potency of these "antimonyall" porringers, we might refer the question to the Section of Therapeutics as to whether their use should not be revived in these days of intestinal stasis? If approved of, they might, particularly if combined with the "Perpetual Pills, become popular, especially nowadays when economy and thrift are so much called for. Only our pharmaceutical friends and the manufacturers of paraffin emulsion might deplore such a revival.

In conclusion, I apologize for butting into a Section so learned as this with a communication so trivial. My excuses are based on the kindness of my friends—Mr. de Navarro, who has entrusted me with these two unique specimens of *Pocula Emetica*; Dr. Singer, who has furnished me with so much lore on the matter; and Sir Herbert Jackson, whose modern scientific investigations have enabled us to verify the empiric practice of three hundred years ago.

BIBLIOGRAPHY.

BALME, "Mémoire contenant quelques réflexes sur l'usage des vomitifs dans le traitement des maladies aiguës," *Journ. de Med., Chir., Pharmacie*, Aoust, 1769, xxxi, p. 123. BASIL VALENTINE, *The triumphant Chariot of Antimony*, London, 1678. CABANES, *Remèdes d'Autrefois: L'antimoine*, Paris: A. Maloine, 1910. REDWOOD, "Note on *Pocula Emetica*, emetic cups, or cups of antimony," *Pharmaceutical Journal and Transactions*, xviii, 1858-59, No. 1, p. 18. POMET, *A Compleat History of Drugs*. Written in French by Monsieur Pomet, Chief Druggist to the late French King Lewis XIV. Done into English from the Originals. The Third Edition, London, 1717. FRANCIS R. PACKARD, M.D., *Guy Patin and the Medical Profession in Paris in the XVIIth Century*. London: Oxford University Press, 1924.

Section of the History of Medicine.

President—Dr. J. D. ROLLESTON.

Celsus' *De Medicina*—A Learned and Experienced Practitioner upon what the Art of Medicine could then Accomplish.

By W. G. SPENCER, M.S., F.R.C.S.

INTRODUCTION.

As a monument marking a station on the highroad of the History of the Art of Medicine, Celsus' *De Medicina* has in recent years undergone depreciation, the author being held to have been himself not a practitioner of the art, but the compiler of an encyclopædia of which the portion on medicine is alone extant, other parts on Agriculture, the Military Art, Rhetoric, Philosophy and Jurisprudence being known only through quotations by Columella, Quintilian, and others.

Writers on the history of medicine have convinced themselves that the author was not himself a practitioner by considerations external to the text of the work; I cannot but think that Sir Clifford Allbutt in his FitzPatrick Lectures yielded somewhat to this view. On the other hand I feel supported by contrary observations of Sir William Osler in asking for a hearing on account of the importance of the opinion I advocate. I must, however, excuse myself on the score of time from countering negative arguments, for I recall to notice indications supplied by the text that the writer was himself an actual practitioner of the art; these quotations from the text supply evidence of such a superior character as to wave aside those of a lower grade drawn from reasonings external to the work.

If I use the name Celsus, it is without prejudice; it is the name at the head of the archetypal manuscript which came to light shortly before the era of printing. As to an anonymous author I simply refer to what has been written on the subject of anonymity in connexion with ancient books.

I have used the most recent revisions of the text by Daremberg, and by Marx, including the latter's references to book, chapter and paragraph. If in translating I vary from the eighteenth century translation by Grieve I do so with all respect; I have found assistance in del Lungo's translation into modern medical Italian as a sort of lift half way to English. Chiefly I have aimed to keep up an agreement between the various corresponding passages, as also with the numerous references to Hippocrates, translated by Littré, Fuchs, and by W. H. S. Jones in the two volumes he has already published in the Loeb Classics. Assuming the writer to have been himself a practitioner of experience, when rendering his statements into English, one has supposed that he wrote what would make sense from the medical point of view.

In more than one hundred places, scattered throughout his work, the writer used the first person singular or plural. I propose to quote some of these passages, along with their immediate contexts, to show that the observations are derived from an actual experience of medical practice.

The importance of the view I advocate is that this work is the only source of information as to the actual practice of the art of medicine at the time it was written, under the reign of Tiberius, when Roman civilization had reached its height, just after the Republic had changed over to the Empire.

It propounds opportunities which persons were given, provided at any rate that they had at their command wealth and leisure, of keeping themselves in health, and of getting cured from certain diseases and accidents. It implies that these opportunities were available at such centres as Rome, Alexandria and Pergamos. Medical officers accompanied the legions to the confines of the Empire. Scribonius Largus, who quoted Celsus, attended Claudius on the invasion in A.D. 43 which was followed by the conquest of Britain. Henry Barnes in 1914 brought before this Section the inscription found at Borecovicus, now in the Newcastle Museum, to the memory of Anicius Ingenuus, Medicus Ordinarius of the first Cohort of the Tungrians, who had gained that mark of affection although only aged 25 at his death.

On Trajan's Column, A.D. 113, the medical officer is shown completing the bandaging of the soldier's wound. It is only from Celsus that we can learn how the wounded were then actually treated, how the arrow and spear heads and the leaden balls were removed, how the wounds were dressed and the complications countered. It is indeed arguable that Paulus Aegineta had before him the description by Celsus; Paulus was followed by Abulkasim, by the Italian surgeons, and by Paré.

The *De Medicina* is a uniform whole with an absence of signs of re-editing, additions or transpositions. There is a continuous system of referring both backwards and forwards, as well in the case of generalities as of details. It is a collection of statements: that patients could be and were being cured of certain defined diseases and accidents, that other diseases and accidents were incurable; that it was the duty of the practitioner not to undertake, nor even to incur or assume responsibility for cases which the art could not relieve because such action on the part of the practitioner tended to be derogatory to the art.

The following quotation is general to the whole work:—

"In his relation to the lesions of the body, however, the practitioner ought to recognize all those which may be incurable, those which may be cured with difficulty, and those the more readily curable. For it is the part from the first of a prudent man, not to touch a case he cannot preserve, and not to risk the appearance of having killed one whose lot is but to die. Again, when there is grave apprehension without, however, absolute despair, he will point out to the relatives of the patient the hope there is in the midst of difficulty, for then if the Art is overcome by the malady, he will not seem to have been an ignoramus, nor to have erred.

"While such steps become a prudent practitioner, on the other hand it is the way of a boaster to exaggerate a small matter in order that he may seem to stand out the more. It is equally obligatory, in such an instance, to make also a prompt statement, and with even greater care to pay attention, lest what is itself little may be made more by negligence in the curing of it." (V, 26, 1 C.D.)

The writer, in dealing with medicine as one of the arts, exhibits a special Roman merit, that included under the term *gravitas*, as also the peculiar sense of *decorum* which had descended from Hippocrates, and which he shows whenever dealing with the *partes obscenæ*. He is thus in marked contrast with classical writers of the time, translators of whom are obliged either to omit to translate passages or to translate into some other modern language, or intentionally to mistranslate. In some measure the *De Medicina*, taken as a whole, serves as a corrective to the bad opinion held of Roman society.

It is abundantly evident throughout that the writer's practice had lain among the upper classes; the underlying assumption is that the patients were in the possession of wealth and leisure, with literary tastes and education, not engaged in manual labour. The references to housing, food and drink, exercises and games, travel to escape pestilence, a cure at mineral water resorts, are all in accord—as also are the measures included under the term *gestatio*, i.e., the shaking of the patient, whether in a bed upon rockers, or in a slung hammock, or the jolting in a litter or chariot or on horseback, rocking in a boat at anchor, or tossing on board a sailing ship. The pharmacopœia included a number of drugs from the East as far off as

India; the prescriptions involved an elaborate compounding by skilled pharmacists. Patients are assumed to have the means either of purchase at apothecaries' shops or to have an educated slave as dispenser.

The following relates to the practitioner's first visit:—

"Thus, at the practitioner's first visit, the solicitude of the patient, who is in doubt as to what may turn out that he has the matter, disturbs his pulse. On this account a practitioner of experience does not forthwith seize with his hand the patient's forearm but at first sits down and with a cheerful countenance inquires of the patient how he does. And if the patient is alarmed he calms him with entertaining talk, and only after that moves his hand to the patient." (III, 6, 6.)

The *De Medicina*, as compared with the Hippocratic Collection, has a restricted aim. It is concerned with that part of medical science which the Greeks had named "Therapeutike" (sc. *Techne*), under three headings: "Diatetike," "Pharmakeutike," and "Cheirurgike." Other parts, Semiotics and Prognostics, are included only just as far as necessary to define the treatment to be adopted and the cases to be undertaken.

The Proemium (meaning according to Quintilian an entering upon the subject to be described) which commences the First Book, gives in outline a history of the art brought down to Asclepiades and his immediate followers; altogether in the course of the work seventy-two names of authorities are mentioned. This is followed by a running commentary upon the practice of the writer's contemporaries, with which he exhibits a comprehensive acquaintance. He had before him the Hippocratic Collection not different from that which has come down to us. He treated Hippocrates as the sole author, and in some twenty passages speaks of him in terms of special praise. Indeed, the *De Medicina* is, to a considerable extent, an applied commentary on the Works of Hippocrates, but without direct copying; an independent judgment is exercised, and there are omissions. Nearly all the Aphorisms are given particular interpretations and applications. The Prognostics and Prorrhethics are used so far as the writer needed. His Eighth Book is a summary of the great treatises on Injuries of the Head, Fractures and Dislocations.

The contemporary practice of medicine varied with the sect to which the practitioner professed to belong. Those who held that the art should be based on reasoning, a *medicina rationalis*, claimed for themselves a knowledge of the "Nature of Things" (Gr. *φύσις* "how things come about") in accordance with the dogmas of the Greek philosophers. These Rationalists propounded as requisites a knowledge: (1) of hidden causes; (2) of evident causes; (3) of natural actions, i.e., what we now call physiology; (4) of the internal parts, i.e., anatomy. Others based their practice upon the experiences gained by observations on individuals. These Empirics restricted their attention to evident causes, contending that questionings about obscure causes and natural actions were of no use because nature is not to be comprehended. The followers of Erasistratus had developed what they termed a "Methodos" or "Way." They contended that there was no cause whatever, the knowledge of which had any curative bearing; it was sufficient to observe certain general characteristics of all diseases which they grouped into three classes, one constriction, another relaxation, the third an intermediate mixture of the two forms—a *medicina contemplatrix* of those characteristics which diseases have in common. These Methodists dissented from the Rationalists because they were unwilling that the art should consist in conjecture about hidden things, and from the Empirics because they thought that in the mere observations of experiences there was little of the art of medicine.

There is an erroneous statement copied by one from another that the *De Medicina* was written for owners of *latifundia*, who had *valetudinaria* (Gr. *paionia*) for their slaves. It is just the reverse of the truth. Throughout there is an underlying assumption that patients possess means and leisure. The only mention of valetu-

dinaria is in the following passage in which Celsus gave his opinion against the practice of the Methodists.

"For both those who treat cattle and horses, because they cannot learn from dumb animals particulars of their complaint, attend only to common characteristics; and also foreigners, in their ignorance of subtle reasoning in the Art, look rather to the common ones. Again, those who take charge of large valetudinaria, because they cannot pay full attention to individuals resort to those characteristics which diseases have in common." (Proem 65.)

After quoting Hippocrates, Celsus concluded:—

"Hence I contend that he who is not acquainted with the peculiar characteristics has merely the general ones to learn from. He who can become acquainted with the peculiar ones, ought not to neglect generalities whilst insistent as well upon the peculiarities. With a knowledge of each on a par, it is more useful to have in the practitioner a friend rather than a stranger." (Proemium 73.)

In discussing the mean to be observed between prudence and rashness there was the use of conjecture as to obscure causes, for in one sense medicine was an *ars conjecturalis*. The case quoted by way of illustration further exhibits acquaintance with practice among the upper classes.

"More rarely, yet now and again, disease has about it something novel. That this does not happen is manifestly untrue, for in our time a lady from whose genitals a fleshy mass had prolapsed and become gangrenous, died in the course of a few hours, whilst physicians of the highest standing found out neither the kind of malady, nor a remedy. I conclude that they attempted nothing because no one was willing to risk a conjecture of his own in the case of a distinguished personage, lest he might seem, unless he had saved, to have killed her. Yet it is very likely that something might possibly have been thought of, had no such shyness prevented, and perchance had that something been tried, it might have saved her." (Proemium 49, 50.)

A passage torn from its context continues to be quoted repeatedly as an opprobrium by these who would try to defame in one or other aspect the art of medicine. In Alexandria, executions were carried out by thrusting the wretch backwards, slitting open the hypochondria and diaphragm, and tearing out the heart and other viscera. Cortez found it the customary mode in Mexico, and this execution was continued in Europe during the eighteenth century. In this country, David the Welsh Prince, Wallace the Scot, Garnett the Jesuit, in front of St. Paul's, Catesby of the Gunpowder Plot, Harrison the regicide, were executed in this way. Despard, in 1803, after being sentenced to it was drawn on a hurdle to Newington, but the crowd was disappointed, for he was first beheaded. The Fenians, in 1866, were condemned to it but the sentence was not carried out. In Roman times the Augurs flayed living animals, but there are exceptional instances in which living men were so sacrificed. It would seem that some of the Alexandrians attended these executions in order to make observations.

"It is no cruelty, say they, that criminals; and they but a few, whilst they are being executed, should be searched for ways of remedying innocent people of all future ages." (Proemium 26.)

Vesalius, 1500 years later, in Padua, received the heart from the executioner, and ran with it into an apothecary's shop, where he observed its beatings. But Celsus proceeded to use the strongest expressions in condemnation of the practice.

"Most atrocious," "with so much violence," "mangling," "folly," "assassinating medical practitioner," "dire cruelty," "tearing to pieces," "repellent," "a cruel cut-throat." "If, however, there be anything to be observed whilst a man is still breathing, chance often presents it to the view of those treating him. At times, a gladiator in the arena, or a soldier in battle, or a traveller who has been set upon by robbers is so wounded that some or other interior part is exposed in one man, another in another. Thus, a prudent practitioner learns to recognize site, position, arrangement, shape, and such-like, not when destroying life, but when restoring to health. He learns in the course of a work of mercy what others would come to know of by means of dire cruelty." (Proemium 42, 43.)

The Proemium ends with this summary :—

"I return, then, to what I myself propound. I am of opinion that the Art of Medicine ought to be based to some extent on theoretical reasoning, but be grounded essentially upon evident causes, all obscurities being rejected from the practice of the Art, although not from the cogitations of him who exercises the Art. To cut open the bodies of living men is as cruel as it is needless; of the dead it is a necessity for learners, who should know positions and relations which the cadaver exhibits better than does a living and wounded man. The remainder, which can be learnt only on the living, actual practice will demonstrate in a somewhat slower, yet much milder way, in the course of caring for the wounded." (Proemium 74, 75.)

DIAITETIKE.

Of the three divisions of the art, *Diaitetike* had ranked the highest, and the most famous authorities had been its exponents. It had a wider scope than what we now generally include under Dietetics. In addition to the varieties of food and drink for the sick of which Celsus gives his own classification, and the precise occasions when these should be administered, there was the subject of Hygiene; how a man, whether in good or in poor health, should protect himself and escape the influence of seasons, weather, climate, soils, and endemic and epidemic fevers. Celsus has in view Romans approaching middle age, prone to eat and drink overmuch, and to take too little exercise. Under Dietetics were also included the Common Remedies, *communia auxillia*, viz., blood-letting and cupping, purgation, emesis, rubbing and anointing, fomentations and baths, gestatio and exercise. These common remedies were assumed to be so well known that, as distinct from surgical operations, no descriptions of the actual carrying out are given, only the indications and precautions relating to each common remedy.

The opening paragraph of Book I and the final one of Book IV complete the circle of the dietetic regimen traversed as it were by the patient.

"A man in health who is vigorous and his own master should be under no obligatory regimen and have no need for a physician nor for a rubber and anointer. His kind of life should afford him variety, he being at times in the country, at times in town, but more often in the open; at times to sail, to hunt, at intervals to rest, but the more frequently to take exercise. For whilst laziness weakens the body, work strengthens it; the former brings on premature old age, the latter prolongs youth." (I, I, i.)

Then at the end :—

"Even after complete recovery, a sudden change in his life will be risky, and may be a cause of disorder. Therefore he should only little by little leave off what has been prescribed, in the course of passing to a life of his own choosing." (IV, 32, 2.)

A general characteristic of the writer was moderation, the adoption of the mean between two extremes. I quote passages relating to the maintenance of health.

"But whilst exercise and food to the amount as above are necessities, the diet of athletes is a harmful excess, for should there be an interruption in the training, owing to necessities of civil life, it affects the body, and bodies which are thus customarily overfed age very quickly and become infirm." (I, I, 3.)

"I note that emesis was rejected by Asclepiades in the book written by him entitled, *De tuenda sanitate*. I do not blame him for being disquieted with the custom of those who by emesis every day subserve their gormandizing faculty. He has even gone somewhat further, for from the same volume he has likewise expelled purgings, which indeed are pernicious when procured by too powerful medicaments. Such measures are not, however, to be dispensed with entirely, for there are conditions and constitutions, times and seasons, which can make them necessary, provided that they are employed in moderation and only when needed." (I, 3, 17.)

"I believe on the ground of experiences that emesis is now and then proper, nevertheless with this reservation that no one who wants to keep well and live to old age should make of emesis a daily habit." (I, 3, 21.)

To provoke a vomit Celsus prescribed a radish on an empty stomach, exceptionally the root of *Veratrum album*.

Another "Common Remedy" was the bath, and special care was needed to avoid what we call heart failure.

"On arriving at the Bath he should sit in the Laconium [the sweating room] for a while to try whether his temples become tightened, or whether some sweating arises. When the former happens, it should not be followed by the bath, which for that day is unserviceable. The patient should be anointed and carried home; cold of every kind is to be avoided and fasting practised. But when his temples are unaffected and sweating starts first upon them, and then elsewhere, his face is to be bathed with hot water; then he should get unto the Solium [hot bath] where it is to be noted whether the skin wrinkles. This can hardly happen when the preceding indications have been attended to, but it is a sure sign that the bath is then unserviceable." (II, 17, 6.)

In Book II are given the signs, *signa*, Gr. *semeiotika*, of impending disorders, *præcedentes morborum*, Gr. *prodromata*, and the degree to which the signs gave rise to apprehension. This is followed by the signs of the actual starting of disease, its increase, acme and decline, ending in convalescence, together with, in each instance, the prognosis good or bad.

The dietetic regimen laid the greatest importance upon fasting, *abstinencia*, Gr. *asitia*, at the commencement of illness.

"Of fasting there are two varieties, one where the patient takes nothing at all, the other, nothing unless what is suitable. The beginnings of diseases desiderate hunger and thirst, established diseases moderation, so that nothing but what is expedient, and not too much of that, is consumed—surfeit following a fast is improper; what if it be unserviceable for men in health upon whom some necessity has imposed hunger, how much more unserviceable for a sick man. To a sufferer nothing is more advantageous than a timely fast." (II, 16, 2.)

The signs of death, approaching or actual, presented the greatest difficulty, aggravated by a hasty funeral, before decomposition had become evident.

"I know that I may be questioned by someone on this point; if there are such ascertained signs of approaching death, how is it that patients who have been deserted by their medical attendants have at times recovered, and rumour has spread it about that some have revived whilst being carried out to burial. Democritus, a man justly renowned, held that there are no sufficiently ascertainable signs of life having ended upon which practitioners should rely; hence he did not admit that there could be any certain signs of approaching death. To Democritus I might reply that approximate signs often deceive inexperienced practitioners but not good ones. Asclepiades, when he met the funeral procession, recognized that the man who was being carried out to burial was alive, and a fault of a professor is not primarily a fault of the Art. With more precision, however, I will submit this, that the Art of Medicine is a conjectural one, and such is the characteristic of a conjecture that, whilst it answers in a measure the more often, yet it is deceptive at times. A sign which answers in countless patients, and is deceptive scarcely in the thousandth case, is not therefore to be rejected." (II, 6, 13-16.)

The allusion is to Asclepiades who, meeting the funeral, is said to have recognized that the man was alive by feeling his pulse. Pliny dilates on the dangers of premature cremation.

Book III is concerned with the curing of various general diseases, acute and chronic. Of these, periodic fevers held the first place. A closely reasoned description implies the assiduous attendance of the practitioner in order to observe the indications required by the dietetic regimen, viz., variations in the surface temperature, especially of the extremities, and of the changes in the strength of the pulsations at the wrist. I quote some of the writer's observations.

"Asclepiades said that it is the office of the practitioner to cure with safety, speedily and pleasantly. Agreed, but generally both hurry and easy going are apt to be dangerous." (III, 4, 1.)

"Now I concede that medicinal purges and clysters should be administered, yet but seldom, and I reckon that they should be administered so as not to destroy the strength of the patient, for there is very great danger from weakness." (III, 4, 3.)

"In fact the best medicament is food, opportunely given; the question is when should it be given first." (III, 4, 6.)

"Hence it can be understood that it is not possible for many patients to be cared for by one practitioner; provided that he is skilled in the Art, he is the proper one who does not absent himself much from the patient. But they who are subservient to gain, since the more is to be got out of the many, adopt freely those precepts which do not enact a sedulous attendance." (III, 4, 9, 10.)

"For these reasons (in cases of quotidian and hemitertian fevers) I delay to give food until midnight, i.e., when one worst time is over, and the next furthest off, whilst the following hours before dawn are those during which all patients generally sleep the most; after that comes early morning, naturally the period of most relief." (III, 5, 6.)

Celsus throughout makes the patients' strength a primary consideration.

"Indeed the *Morbus Cardiacus* is nothing other than excessive weakness of the body which by inordinate sweating becomes dissolved, the stomach being languid. One may recognize it at once by the exiguous and weak pulsation of the blood vessels, and by the sweating which is both uncustomary, excessive and untimely."

After prescribing methods for reducing sweating, and for administering food and wine on a weak stomach, the writer concludes:—

"The last resource to support the patient's strength is the introduction into the bowel from below of barley or spelt gruel." (III, 19, 5.)

Later writers, Pliny and Oribasius, said that nutrient enemata were first used by Lycus of Neapolis; their general use is of quite recent date.

The following quotations are in reference to special disorders.

"The insane, however, are to be agreed with more often than opposed, and their mind, unperceived by them, is to be gradually turned from talking foolishly to something better. Their interest should be awakened from time to time, as may be done in the case of men fond of literature. Some who were refusing to take food were induced to do so by being placed on couches between other diners." (III, 18, 11.)

On the question of paracentesis for *Ascites* in relation to the liver:

"I do not ignore that this way of cure was disapproved of by Erasistratus, for he deemed the disease to be one of the liver, that therefore it was the liver which had to be rendered healthy, and that it was no use to let out water which will be reproduced by that organ being diseased. The disease, however, is not primarily one of that organ alone, the spleen also is affected, and there is cachexia of the body in general. Further, unless evacuated, the watery fluid, unnaturally collected there, comes to be of harm to the liver and rest of the internals." (III, 21, 15.)

For phthisis Hippocrates recommended mountain air, Pliny a stay in pinewoods, Aretæus sea air, Galen milk in the mountains, Celsus a long sea voyage at the earliest stage.

"But if there is a worse illness and a true phthisis, it is necessary to counter it forthwith at the very commencement, for it is not readily overcome when of long standing. If the strength allows of it, there is need for a long sea voyage, a change to a climate more dense than that which the patient is quitting, hence the most suitable is the passage from Italy to Alexandria." (III, 22, 8.)

PHARMAKEUTIKE.

The Section of Pharmaceutics occupies Books V and VI, divisible into a Proemium; Chapters 1-16 Medicaments as simples, classified according to their topical application; Chapters 17-22 simples compounded for external use; Chapters 23-25 prescriptions for internal use; Chapters 26-28 treatment of wounds. Book VI, local lesions likewise treated mainly by topical applications.

The Proemium commences:—

"I have spoken of those bodily disorders in which dietetics afford the most aid; I pass on to that part of Medicine which combats them rather by medicaments. To these ancient writers attributed much, both Erasistratus and those who styled themselves Empirics, especially, however, Herophilus and those who were guided by that man, inasmuch that they treated no kind of disease without medicaments. On the other hand Asclepiades dispensed for the most part with the use of medicaments, not without reason, for nearly all medicaments harm the stomach and are kakochylous."

"Be it that in many dietetics are the most useful, yet in some measure diseases do occur to some extent in our bodies which cannot without medicamenta be conducted to a cure. Before all things it is well to recognize that all parts of medicine are so interconnected, that it is impossible to separate any one part from the whole, but each part of the art of medicine gets its name from that of which the most use is made. As therefore the branch of dietetics has recourse at times to medicamenta, so that which combats particularly by medicamenta should adopt also that of dietetics, a course of much advantage in all disorders of the body." (V, Proem, 1-3.)

Asclepiades gained the nicknames of "Water doctor," "Wine giver." His notion approximates to the view that all the *materia medica*, taken internally, are poisons more or less diluted.

In Book VI there are mentioned Cutaneous Lesions, particularly on the scalp and face, and attention has been given to these passages by those interested in dermatology. Erasmus Wilson identified many of the lesions, but found difficulty with others, for all ancient writers gave inadequate descriptions, except as regards variations in colour. Precise descriptions supplemented by illustrations are of quite recent date, but there is one which serves to confirm the practical knowledge of the writer. It relates to the serpiginous alopecia he named "ophiasis," from *ophis* a snake, and *alopecia* presumably derived from the appearance of a mangy fox (Gr. *alopea*).

"That which is named Alopecia spreads out in an ill-defined configuration. It occurs both in the hairy scalp and in the beard. That form which from its similitude is called Ophis, commences at the back of the head, it does not exceed the breadth of two fingers; it creeps forwards to the ears by two heads, even in some to the forehead, until the two heads join one another in front. The former affection occurs at any age, the latter generally in young children. The former scarcely ever terminates except under treatment, the latter often by itself." (VI, 4, 2.)

Now this form of alopecia termed "ophiasis" was definitely identified by Sabouraud in 1898. He exhibited nineteen Paris school children, all affected as described by Celsus. The ordinary duration was eighteen months; it might go on to complete baldness, but in the great majority of cases it had healed spontaneously by puberty.

CHEIRURGIKE.

Cheirurgy, or treatment by manipulation and operation, occupies Books VII and VIII, concerning which there is no difference of opinion; throughout there is evidence of experience in the actual practice of surgery.

Gurlt, whilst stating that German authorities had held that Celsus was not a practitioner of medicine, is forced in connexion with surgery to observe "the description of several surgical operations is so methodical, clear and thorough, that one is forced to hold it for impossible that he had not seen some, if not all of them carried out, or himself had carried them out."

It is indeed impossible to suppose otherwise when the descriptions are considered of the operations for the removal of missiles, ingrowing eyelashes, or couching of cataract, of those on the groin and scrotum for reducible hernia, hydrocele and varicocele, of the lithotomy operation with its complications, and the two operations on the female. I select for quotation the Proemium to Book VII, an operation for adhesion of the eyelids, and the embryotomy operation.

"The third part of the Art of Medicine is that which cures by the hand, as is both known to the Commonality and has been stated already by me. It does not indeed omit medicaments, nor the dietetic regimen, but nevertheless achieves most by the hand. What its effects is among all parts of Medicine the most evident.

"If the same dietetic regimen, whilst often salutary, is often of no use, it can be a matter of doubt in the case of maladies in which fortune helps much, whether recovery has been due to the Art of Medicine, or to the well working of the body.

"Moreover, in those cases in which we are dependent chiefly upon medicaments, although improvement by such means is the more evident, yet it is manifest that recovery may be often looked for in vain, and that health is often recovered without their aid. This can be grasped, for instance, in the case of the eyes, which after being in trouble for a long while under doctors at times get well without them.

"But in that part of Medicine which cures by the hand, all improvement, however assisted somewhat in other ways, is for the most part nevertheless to be ascribed to it. This part, although a very ancient one, was more cultivated, however, by that parent of Medicine in general, Hippocrates, rather than by his forerunners."

After brief references to surgeons in Alexandria and in Rome he continues:—

"A Surgeon should be youthful, or at any rate nearer youth than age, with a strong and steady hand, which never starts to tremble, prompt no less with the left than with the right hand, with vision sharp and clear, a spirit undaunted, pitiful but so as to wish to cure the patient whom he undertakes, yet not moved by his clamour: neither hastening more than is desirable nor cutting less than necessary, but all the time doing everything as if no emotion was being excited by the patient's cries."

"But it may be asked what properly may be claimed for this part of the Art, seeing that Surgeons claim for themselves the curing, not only of wounds, but also of many lesions which I have described elsewhere. I, for my part, deem one and the same man able to undertake all such, and be it that divisions are made, I praise him who takes on the most. I have myself reserved for this part wounds made by the surgeon, not taken over by him, further those wounds and ulcerations which I believe to be benefited more by Surgery than by Medicaments, as well as all that concerns the bones." (VII, Proemium, 1-5.)

Operation for Adherent Eyelid.

"At times the eyelids adhere together, and the eye cannot be uncovered. To this affection there is commonly added an adhesion of an eyelid to the white of the eye. The Greeks call both lesions Ancyloblepharus. When simply the eyelids adhere together, they are separated without difficulty, but sometimes in vain, for they again become agglutinated. One should try, however, because it is often a success.

"But when an eyelid adheres to the white of the eye Heraclides of Tarentum originated a method of undercutting with the edge of the knife turned away from the eyeball, yet with great moderation so that nothing is cut away either from the eyeball or eyelid.

"I for my part do not remember anyone to have been so cured. Meges also has related in a tract that he has tried many times, but has never been successful, for the eyelid has always again become adherent to the eyeball." (VII, 7, 6.) ([8] Hirschberg.)

Embryotomy.

I select this operation because it admits of a quotation in continuity without need of commentary.

"When a woman has conceived, if the foetus already at term dies inside and cannot make exit of itself, recourse is to be had to a cure which may be counted among the most difficult, for it requires extreme caution and moderation, and entails the greatest risk. But before everything the wonderful nature of the womb, as in many other matters so in this also, is easily recognizable. To begin with, then, the woman should be placed on her back across the bed so that her iliac regions are compressed by her thighs with the result that her hypogastrium is in full view of the surgeon and the foetus is being forced towards the neck of the womb. This after the death of the foetus contracts and then relaxes a little. The surgeon making use of this opportunity should insert a greased index finger of the right hand which he keeps against the neck of the womb during the period of its contraction until it again opens, when he should insert a second finger, and the other fingers on like occasions until the

whole hand can enter. To allow of this, much depends upon the size of the womb, its sinew-like tissue, the patient's constitution, and also her strength of mind, especially when on occasion both hands have to be passed in.

"It appertains, indeed, to the procedure that the hypogastrium and extremities should be kept very warm, that inflammation has not begun but that the treatment has been adopted forthwith whilst the case is recent. For if the abdomen is already distended, neither can the hand be inserted nor the fœtus extracted otherwise than accompanied by the greatest suffering, followed often by vomiting and by fatal spasm with tremor.

"On inserting the hand the position of the fœtus is first felt, for either it lies head on, or feet foremost, or crosswise, generally, however, so that there is a foot or hand within reach. It is the object, in fact, of the surgeon with his hand to direct the fœtus into a head, or even a foot presentation, when markedly presenting otherwise. And if there is nothing else, a hand or foot being grasped, the trunk is straightened. For the hand converts the presentation into a head one, the foot into feet presenting. Then if the head is first, a hook, otherwise smooth, with a sharp point, is fixed into an eye, ear or the mouth, or at times even straight into the forehead, when by drawing upon it the fœtus is extracted.

"Nevertheless extraction should not be made at any moment, for should this be attempted when the cervix is contracted, there being no way out for the fœtus, the hook tears away and its point then lacerates the cervix; there follows spasm and great risk of death. Whilst, therefore, the cervix is contracted one should rest, and whilst it is gaping draw gently on the hook, and so at these opportunities gradually extract the fœtus. The hook should be drawn upon with the right hand, whilst the left is inserted against the fœtus so as, at the same time, to guide it. It may happen that the actual fœtus is distended with fluid, and from it has discharged foul sanies. If so, the abdomen of the fœtus is bored into by the index finger, so that when by the escape of fluid the fœtus is reduced, it can be delivered by the hand alone. For a hook inserted readily slips out of such softened structure, when the danger noted above is incurred. When the fœtus has been turned to present by the feet, it is also not difficult to extract, the feet being simply grasped by the surgeon's hands it is readily drawn out.

"Should the fœtus be lying crosswise, and it cannot be turned straight on, the hook is inserted into an armpit and traction slowly made, when usually the neck bends, and the head looks backwards to the rest of the fœtus. The remedy is then to cut through the neck in order that the two parts may be extracted separately. It is done with a hook which, whilst resembling the one above mentioned, has all its concavity sharp. This done, one must proceed to extract the head first, then the rest, for if the larger portion be extracted first, the head slips back into the cavity of the womb, when it cannot be extracted without the greatest risk.

"Should this, however, happen a folded pad is placed upon the woman's hypogastrium, and then a strong man, not an untrained one, standing on the left side, should place his hands, one over the other, upon the hypogastrium and so press that the head is forced to the mouth of the womb, where it is extracted by the hook as described above.

"When now one foot presents whilst the other remains behind with the trunk, the cutting away is to be done piecemeal of anything that protrudes.

"If the buttocks begin to engage in the neck of the womb, they are pushed back, and the second foot being found it is then drawn upon.

"There arise indeed other difficulties, as when the firm trunk will not come out, and has to be extracted after being cut up.

"When now the fœtus has been extracted, it should be handed to the male assistant to hold on his upturned hands, whilst the surgeon with his left hand draws gently on the umbilical cord so as not to rupture it, he passes his right along it up to what they call the *secundæ* which are the envelope of the fœtus within the womb. The hand having grasped the entire *secundæ*, including the whole of the fine blood-vessels and membranes, brings them down from the womb in this way and extracts the whole together with any retained blood-clot." (VII, 29.)

CONCLUSION.

I have given quotations from the several parts of the work to show that the author of the *De Medicina* had himself practised the art, and as such had attained an intimate acquaintance with Clinical Medicine. In spite of brevity, restricted

vocabulary with the use of the same word in several meanings, he supplies an intelligent and informed *résumé* which gives direction and application to the Greek Medicine—to the Aphorisms, for example, which may be deemed superior to Galen's diffuse style and philosophical tendencies.

In studying Celsus it is indeed necessary to have continuously in mind the limitations of his knowledge, his scanty acquaintance with human anatomy and the erroneous views of the movement of the blood and humors, and of the brain and spinal cord as little more than marrow of bone.

His imperfect ideas about the various structures is shown by the use of one term *nervus* not only for nerves but also for tendons, fasciae and ligaments; moreover, it is applied to the tunics or coats of the viscera, to the wall of the uterus, to the *vas deferens*, as well as to fibrous tissue forming the wall of an abscess. His knowledge of internal pathological changes was limited to the five classes of lesions mentioned. (V, 29, 1.)

If it is allowed that the author of the *De Medicina* was himself a practitioner of the art, then he is an authentic witness, the sole witness for the period, of what the Art of Medicine was then accomplishing within the Roman Empire.

REFERENCES.

- [1] DAREMBERG, C., *A Cornelii Celsi de Medicina libri Octo*, Lipsiae, 1859. [2] MARX, F., *Corpus Medicorum Latinorum*, i, A Cornelii Celsi quae supersunt, Lipsiae et Berolini, 1915. [3] GRIEVE, J. (d. 1773), "A. C. Celsus, Of Medicine in Eight Books translated with Notes Critical and Explanatory," 1756. [4] DEL LUNGO, A., *Della Medicina—Libri Otto di Aulo Cornelio Celso* Volgaizzamento, 1904. [5] BARNES, HENRY, *Proc. Roy. Soc. Med.*, 1914, vii (Sect. of Hist. of Med.), p. 75. [6] SABOURAUD, Sur l'Ophiasis de Celse, *Annales de Dermatologie et de Syphilographie*, 1898, ix, p. 545. [7] GURLT, E., *Geschichte der Chirurgie*, 1698, i, p. 337. [8] HIRSCHBERG, J., "Graefe-Saemisch Handbuch der gesammte Augenheilkunde," 2te Auflage, 1899, Bd. 12, c. xxiii, p. 274.